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A REVIEW OF THE AFRICAN TRYPANOSOMIASIS PROBLEM

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To be fully comprehended, the vast subject of trypanosomiasis should be examined from three angles—medical, entomological and veterinary. This short review of the whole Pan-African problem is intended for those requiring an overall picture with the minimum of labour, be they newcomers to the subject or highly specialized workers.

The Economic Effects of Trypanosomiasis, Both Past and Present

Little is known about the influences exerted by the tsetse on the people of tropical Africa before the entry of the European powers in the last century. We know that human trypanosomiasis, or sleeping sickness, is a disease of considerable antiquity, a case having been described by a fourteenth-century Arab writer. It seems reasonable, therefore, to assume that epidemics occurred, but possibly they were on a smaller scale than those observed in the first part of the present century: in the days of endless tribal warfare there was little travel, and the population tended to concentrate for safety in large communities, whose extensive farm clearings must have produced tsetse-free zones around the settlements. Animal trypanosomiasis, or nagana, was presumably rife, and owing to a huge, undisturbed game reservoir, was in all likelihood far worse than it is now.

Animal trypanosomiasis has probably exerted a tremendous influence on the development and history of tropical Africa. Why was it that the ox-drawn plough and cart were unknown until the advent of the European? Egyptian influence extended up the Nile, and the culture of the ancient world filtered across the southern edge of the Sahara to Northern Nigeria. (Twenty years ago I bought a necklace in Kano market, which included beads from the tombs of Egypt.) There were also the caravan routes across the Sahara to Morocco, and to the great Songhai Empire in the Western Sudan which, in the early part of the sixteenth century, was highly civilized and even boasted a university at Timbuktu (NIVEN, 1937). Under such circumstances it seems likely that repeated attempts were made to use ox-drawn carts and ploughs, and that these attempts failed because of trypanosomiasis; even now, in marginal lands where cattle can be kept, attempts to set up peasants as mixed-farmers are often a failure, because when the oxen are made to pull a plough their resistance breaks

down and they succumb to nagana (NASH, 1948a). It seems reasonable to suppose that for hundreds of years the tsetse dictated that the economy of the African should be based on the hoe and the head-load, a dictatorship from which only now is he being freed by the petrol engine and railway locomotive.

The southward penetration of Islam and its culture from the Sudan zone would probably have gone far deeper had not the horses of the faithful died of trypanosomiasis. The earlier Portuguese explorers were baulked in their endeavours to settle on the healthier inland plateaux of East Africa, because their transport animals were inevitably killed off by nagana (preface to AUSTEN and HEGH, 1922). Similarly, during the last century, the northward penetration by farmers from the Cape across the Vaal and Limpopo rivers, and beyond, was greatly retarded by the fly-belts (FULLER, 1923).

It would appear that until recently the tsetse fly has played a considerable part in the insulation of tropical Africa from civilizing contacts.

The best example of the direct influence of tsetse on man is afforded by the great Uganda epidemic of sleeping sickness which developed during the years 1902–1905; in Busoga Province alone, some 200,000 people died, or about two-thirds of the population (BUXTON, 1948). Admittedly this was in the days before treatment, but it would be as well not to forget this lesson now that the disease is under control but very far from being eradicated.

Under present conditions, nagana is of far greater economic importance than sleeping sickness; further, it is of much greater medical importance, if the broad view is taken that a deficiency in animal protein among the masses is far more important than a specific disease among the few. The National Research Council of the United States considers that the normal intake of protein should be 80 gm. per day, of which 30 gm. should be animal protein: Dr. B. M. Nicol's findings in the tsetse-infested "middle-belt" of Nigeria show a total intake of 70 gm. of which only 5 gm. is animal protein (NICOL, 1949). Real "meat-hunger" is something which should be seen to be believed: in Tanganyika Territory, I once shot a large zebra near dusk, and left two or three men to guard the carcass overnight; on returning next morning with porters, I was amazed to see how little meat was left: the men had eaten and vomited, eaten and vomited, throughout the night.

The presence of woodland tsetse of various species, heavily infected with trypanosomes picked up from the game, makes it impossible to keep cattle in huge areas of tropical Africa; in other vast stretches, where the challenge is lower, cattle can be kept but losses due to nagana are heavy.

Tsetse flies are also indirectly responsible for producing erosion. Fly-advances into new territory are a common phenomenon, often causing the people to retreat with their cattle into much smaller fly-free areas where over-stocking leads to serious erosion (SWYNNERTON, 1936).

The Background to the Trypanosomiasis Problem

Tsetse flies occupy some 4½ million square miles of tropical Africa (SWYNNERTON, *loc. cit.*), an area that is 1½ times that of the United States of America. This vast area has no common language, communications are normally sparse, and maps are usually inadequately detailed; further, as yet there is a dearth of well-educated Africans willing to work in the field.

The peasant population is understandably slow to accept the revolutionary idea that insects could possibly carry disease, and will remain so until the

masses have been sufficiently educated. I have encountered pathetic instances where the people have moved their village from one bank of a tsetse-infested stream to the other, so as to avoid the evil spirits alleged to have caused a high mortality from sleeping sickness. I have also met children in an advanced stage of the disease, living like animals in the bush, having been turned out of the village because sleeping sickness was held to be highly contagious.

Many of the great cattle-owning tribes are nomadic, here today and gone tomorrow; this does not facilitate treatment of either the owners or the beasts. Some nomads recognize the worst fly-belts, but do not associate their ill-repute with tsetse but with the alleged presence of poisonous herbs or bad water; they will therefore drive their cattle through the fly-belt, not letting them eat or drink in transit. Other tribes recognize the danger of tsetse to their cattle, but, if forced to retreat into an area where the grazing is inadequate, refuse to reduce their herds because the number of cattle owned is a sign of wealth, which is considered more important than the condition of either the beasts or the land.

Such then is the background of the trypanosomiasis problem, a background of vast, under-developed lands in which there is much ignorance; great strides have been made in opening up these lands and educating the peasants, but this progressive movement has still a very long way to go.

Certain Aspects of the Trypanosomiasis Problem

In this section attention will be drawn to certain basic facts which illustrate the complexity of the problem, and mention will be made of some of the latest research findings which are helping us to get an insight into the workings of a great biological complex. In later sections, further aspects of human and animal trypanosomiasis will be considered separately.

Representatives of the genus *Glossina*, of which 22 species are known, are to be found under conditions which range from mangrove swamps and evergreen forests, through woodland savannah of many types, to near-desert; tsetse occur in areas where the annual rainfall is as high as 188 inches, or as low as 15 inches (NASH, 1948a), and at altitudes ranging from sea-level to 6,000 feet (SWYNNERTON, 1936). A knowledge of the habits and climatic and vegetational requirements of each species is needed, if control measures are to be planned intelligently.

Human trypanosomiasis is cyclically transmitted by only certain species of *Glossina*: some species find man unattractive and very seldom attack him. The two types of sleeping sickness, caused by *Trypanosoma gambiense* and *T. rhodesiense* respectively, present different clinical pictures, differ in certain respects in their reactions to therapeutic drugs, and are transmitted by different species of tsetse; yet HOARE (1949) has concluded that the trypanosomes are morphologically indistinguishable, the one from the other, as well as being indistinguishable from *T. brucei* which is non-pathogenic to man but pathogenic to animals, particularly horses and dogs.

All species of tsetse are probably capable of the cyclical transmission of nagana. Under certain conditions, other species of biting flies are believed to spread the disease by "mechanical" transmission; for example, a Tabanid feeding on a heavily infected ox, is disturbed by the beast's tail, settles on an adjacent ox, and plunges in its contaminated proboscis; BUXTON (1955) has reviewed the evidence for this widely-held belief.

All domestic animals are susceptible to trypanosomiasis, but attention will be confined to cattle, which are the beasts of greatest dietary significance; *T. congolense* and *T. vivax* are the main causal organisms, but recent work by GODFREY (1958) suggests that *T. dimorphon* may be of great veterinary importance in Northern Nigeria. Mention must be made of *T. simiae*, which can cause fulminating infections in pigs, animals which in certain parts of Africa provide the main supply of meat.

To turn to the game factor, many species of mammal act as a reservoir of nagana. ASHCROFT (1959a) has collected the records for eastern Africa on the incidence of trypanosomiasis in game; the data are scanty but indicate the potential value of such work: the results suggest that the incidence in some species may be negligible, about 10% in wart-hog and bush-pig, but from 30 to 50% in eland, bush-buck, giraffe, reed-buck, kudu and water-buck.

Game is also important in Rhodesian sleeping sickness. The results of the Tinde experiment, initiated by CORSON (1936), continued by FAIRBAIRN and his colleagues (1946) and later by WILLETT and FAIRBAIRN (1955) and ASHCROFT (1959b), went a long way to incriminate game animals as carriers of *T. rhodesiense*. These workers, starting with a strain isolated from man, and using cyclical transmission by *G. morsitans*, maintained it for 23 years in sheep; the strain was periodically tested in human volunteers and was still infective to man at the end of this long period. They also started a line of this strain in antelope, and before it was lost had demonstrated that its infectivity to man had continued throughout a period of 12 years of maintenance in animals—2 in sheep followed by 10 in antelope of various species (WILLETT and FAIRBAIRN, 1955). Indisputable evidence that game acts as a reservoir for Rhodesian sleeping sickness was obtained in 1958 from a strain of *brucei*-group trypanosomes, isolated from a bush-buck (*Tragelaphus scriptus*) shot in an endemic area in Kenya; a human volunteer, inoculated with this strain, developed the disease (HEISCH, MCMAHON and MANSON-BAHR, 1958).

There is no convincing evidence that game acts as a reservoir for Gambian sleeping sickness; man is certainly the primary, if not the only, mammalian host. Epidemiological studies indicate that man usually contracts the disease at points, such as water-holes, where he repeatedly comes into contact with tsetse. Outbreaks of Gambian sleeping sickness often occur in places which are so heavily populated that there is no game; TAYLOR (1930) describes a good example of such an outbreak.

There is a possibility that domestic animals sometimes act as a reservoir for Gambian sleeping sickness. VAN HOOF (1947) found it easy to transmit a strain of *T. gambiense* cyclically by *G. palpalis* to a succession of domestic pigs, but transmission from pig to fly became progressively rarer until the strain became non-transmissible; the individual pig became incapable of infecting the fly after some months, suggesting spontaneous cure (BUXTON, 1955). In similar work with goats the strain soon became non-transmissible by fly, although one goat remained infective for 11 months (DUKE, 1928). These results are very different from those described for the Tinde experiment.

Game, in addition to providing a reservoir for the trypanosomes of nagana and Rhodesian sleeping sickness, furnishes the bulk of the blood meals for most species of *Glossina*. A study of the host preference of each species of tsetse has recently been made possible by a technique worked out by Weitz of the Lister Institute of Preventive Medicine, London, who, using a combination

of the precipitin test and the inhibition of agglutination test, is able to identify the source of a tsetse's blood meal from a smear on filter paper (WEITZ, 1956). Gorged flies, being inactive, have to be searched for laboriously, so that even for the commonest species of tsetse adequate samples have not yet been collected from a sufficient number of localities to permit of firm conclusions, but some interesting and unexpected results have been obtained, examples of which will be given.

Gambian sleeping sickness is endemic around Kaduna, Nigeria, and *G. palpalis* is the vector, living in the fringing vegetation of streams which traverse the woodland savannah. Of 240 blood meals, identified from 20 localities within 100 miles of Kaduna, nearly three-quarters came from reptiles, man and cattle, at 42, 26 and 5% respectively; excluding cattle, only 15% came from Bovidae and 5% from wart-hog, so that game accounted for only 20% of the sample even in this thinly populated area (WILLETT, 1960).

The picture is entirely different for *G. morsitans*, a tsetse of the woodland savannah, which does not appear to be a vector of Gambian sleeping sickness but is the main vector of the Rhodesian form of the disease in East Africa; of 756 meals identified from two localities near Kaduna, Nigeria, 55% were from Suidae (all wart-hog), and 10% from Bovidae (WILLETT, 1960); of 852 meals from 7 localities in East Africa, 43% were from Suidae (mainly wart-hog), and 38% from ruminants, virtually Bovidae (WEITZ and GLASGOW, 1956); in West Africa game accounted for 65% of the feeds and in East Africa for 82%. So marked a preference for the Suidae is a most unexpected result. More detailed examination of the East African figures shows that of 8 species of antelope, giraffe, buffalo, elephant and rhinoceros, no single species provided more than 5% of the total feeds, and that zebra, hartebeeste and topi appear to be unattractive in that no feeds were recorded from them. The question which now arises is whether it is really necessary to kill *all* species when game destruction is used to control *G. morsitans*, a subject which will be referred to later.

There are also indications of strong host preferences occurring in other species of tsetse; records for the first 4 species given in the table are from East Africa, and for the last 3 from West Africa.

Species	*No. of meals identified*	*Most favoured host*	*Reference*
G. swynnertoni	228	42% Wart-hog (*Phacochoerus aethiopicus*)	WEITZ and GLASGOW, 1956
,,	203	54% Wart-hog	WEITZ *et al.*, 1958
G. longipennis	336	74% Rhinoceros (*Diceros bicornis*)	WEITZ *et al.*, 1958
G. austeni (Zanzibar)	187	88% Bush-pig (*Potamochoerus koiropotamus*)	WEITZ and GLASGOW, 1956
G. pallidipes	68	63% Bush-buck (*Tragelaphus scriptus*)	WEITZ and GLASGOW, 1956
,, (females only)	217	63% Bush-buck	EATRO, 1959

Species	*No. of meals identified*	*Most favoured host*	*Reference*
G. longipalpis	186	67% Bush-buck	JORDAN *et al.*, 1958
G. fusca	158	68% Bush-buck	JORDAN *et al.*, 1958
G. tabaniformis	109	65% Red-river-hog (*Potamochoerus porcus*)	JORDAN *et al.*, 1958

In these examples the host preference is very pronounced, but evidence is accumulating which suggests that where the normally selected host is absent or rare, the fly may favour another species. *G. pallidipes* from East Africa and *G. longipalpis* from West Africa are very closely related species; it will be seen that they seem to share the same preference for bush-buck. It is worth recording that 20% of the *G. tabaniformis* blood meals, referred to above, were from porcupine, a most unexpected second choice.

Much space has been devoted to the topic of host preference, but I feel that Weitz's work has opened a gateway to the more intelligent control of both the vector and the disease. For example, if one knew that in a certain bad area for Rhodesian sleeping sickness the local vector was taking the bulk of its food from a certain host, and if one knew that *T. rhodesiense* could be maintained in that host without loss of virulence to man or transmissibility by the tsetse, it would seem logical to plan the destruction of that host with a view to destroying both the most likely trypanosome reservoir and the vector's most favoured source of food.

The natural infection rate in tsetse flies is another factor which must be considered. The members of the *brucei* sub-group (*T. brucei, gambiense* and *rhodesiense*) pass through a more complete cycle in *Glossina* than do the common nagana-producing trypanosomes, in that they have to reach the salivary glands if cyclical transmission is to take place. A study by the dissection of wild flies of the natural infection rate of either *T. gambiense* or *T. rhodesiense* is unprofitable, because the number of positive salivary glands found is exceedingly small, even in places where sleeping sickness is rife. In both Gambian and Rhodesian sleeping sickness areas, a salivary gland infection rate of 0·8% would scribed block of rain forest (NASH, 1959):—

In the case of nagana, mature infections of trypanosomes of the *congolense* group are found in both proboscis and midgut, and of the *vivax* group in the proboscis only; in these groups, especially in the latter, the cycle is completed in a much greater proportion of flies, and much higher infection rates are found. The rate may vary greatly among the different species of tsetse present in the same area of bush: for example, PAGE and JORDAN obtained the following figures by the dissection of flies caught over the same period in a circumscribed block of rain forest (NASH, 1959):—

	Dissected	*Infected*
G. tabaniformis	3,131	3·2%
G. fusca	808	13·4%
G. nigrofusca	130	25·4%

The very low infection rate in *G. tabaniformis* could be explained either by the tsetse, or by its preferred host, being highly resistant to infection; similarly,

the very high infection rate in *G. nigrofusca* could be due either to the tsetse, or to its favoured host, being highly susceptible. At present, all we know is that *G. tabaniformis* appears to favour the red-river-hog, and *G. nigrofusca* the bush-buck, but we have no certain knowledge of the relative infectibility of the two species of tsetse, nor of the relative susceptibility to infection of the two hosts. Such fascinating problems await solution, and can be solved now that the preferred hosts can be determined.

I would like to see an investigation undertaken by a team of scientists whose object would be to explore in a single area all the factors comprising the biological complex. First they would have to ascertain the population density, infection rate and host preferences of each species of tsetse present, and then collect data on the natural incidence of trypanosomiasis among the favoured hosts. Parallel work in the laboratory would consist of comparative studies of the infectibility of each species of tsetse and of the course of the parasitaemia in captive specimens of the favoured hosts. Having achieved a thorough understanding of the existing biological complex, the investigators would then systematically destroy the preferred hosts, species by species, observing the effect on fly numbers, changes in the host preferences as the most favoured species were destroyed, and the effect on the infection rate in the different species of tsetse. Such an experiment would be very costly, very difficult, and would take a long time to complete, but the results should reveal the fly-host-parasite relationship, which will never be revealed by exploring individual facets of the problem in different parts of Africa.

Human Trypanosomiasis

It is generally accepted that there are two types of human sleeping sickness, the Gambian and the Rhodesian; if a considerable number of cases are seen the two diseases can be distinguished, but in a single case this may be impossible, either clinically or by the study of the parasite (BUXTON, 1948). *T. gambiense* typically gives rise to a disease which runs a relatively chronic course, involves the central nervous system, and produces the symptoms described as " sleeping sickness "; many years may elapse before death. In contrast, *T. rhodesiense* infection normally results in a far more acute disease, with symptoms of severe toxicity, which often culminate in death after only a few months; the rapid progress of the illness gives insufficient time for the development of the classical cerebrospinal symptoms (WILLETT, 1955).

Gambian sleeping sickness occurs throughout western and central tropical Africa, extending to Lakes Victoria and Tanganyika; but the Rhodesian type is confined to the eastern side of Africa, occurring in Ruanda-Urundi, Uganda, Kenya, and extending southwards through Tanganyika, Portuguese East Africa, the Rhodesias, as far as Bechuanaland.

Gambian sleeping sickness presents the problem of greatest magnitude, because the disease is more widespread and the cases far more numerous; but the Rhodesian disease presents a more acute problem, necessitating an even greater degree of vigilance, because an epidemic, such as the one described by MACLEAN (1926), can result in speedy devastation if unchecked.

Gambian sleeping sickness is carried by *G. palpalis* and *G. tachinoides*, which frequent the specialized vegetation lining the banks of streams, rivers and lakes throughout the savannah woodland; both species are often found in heavily populated areas where there is no game. The disease sometimes occurs in the

forest belt, especially under drier conditions, and here *G. palpalis* may be considered to be the sole vector.

Rhodesian sleeping sickness is carried mainly by *G. morsitans*, and to a lesser extent by *G. swynnertoni*, species which rove throughout the woodland; both are closely associated with an abundance of wild game, so that Rhodesian sleeping sickness tends to be confined to areas which are thinly populated by man; game animals can act as a reservoir for *T. rhodesiense*. *G. pallidipes* has also been incriminated (MACKICHAN, 1944), and has been shown by ROBERTSON and BAKER (1958) to be the major vector on the north-eastern shores of Lake Victoria.

Lastly, in this catalogue of differences, *T. gambiense* is normally sensitive to arsenicals such as tryparsamide, whereas *T. rhodesiense* is usually resistant.

Gambian Sleeping Sickness

The course of normal *gambiense* infection has been briefly described, but it should be noted that in the years when Nigeria was experiencing epidemic sleeping sickness, a high incidence of mild trypanosomiasis was frequently associated with serious depopulation (MCLETCHIE, 1948): of Lester's 3 broad categories—mild, nervous and toxaemic—it was the mild form that gave a high proportion of the deaths. MCLETCHIE (*loc. cit.*) did not attribute the majority of deaths to lowered general resistance and intercurrent infection, but believed that: ". . . . a very considerable proportion of deaths, apart from advanced cases, arises from acute toxaemic exacerbation of the actual trypanosomiasis. The mild infection may be slowly progressive as regards involvement of the nervous system, but sudden breakdown, with high fever and toxaemia, occurs in patients who have had the usual minor manifestations of the disease for months or even years. . . . Most of these cases die unseen and untreated". He emphasized the importance of seeking out and treating these mild cases, in persons who would not seek treatment voluntarily. In Uganda, *gambiense* infection has also been described as mild, but fatal (BROWN, 1938); in the early days of the Kissi epidemic in Sierra Leone the same association of mild cases and depopulation was observed (HUTCHINSON, 1954). Some years later, when the incidence in Nigeria had fallen considerably, MCLETCHIE (1953) stated that it was clear from clinical symptoms that many of the strains were invading the nervous system at an earlier stage, were more resistant to treatment, and prone to relapse.

Diagnosis

The technique of preliminary diagnosis in its fullest form includes questioning of each person for symptoms, blood films, gland palpation and puncture, and lumbar puncture of suspicious cases to detect any cerebrospinal fluid changes.

Curative Treatment

It was concluded at the 6th Meeting of the International Scientific Committee for Trypanosomiasis Research, 1956, that the best drug for use at all stages of the disease, and for cases that have relapsed after treatment with other drugs, is Mel B (Arsobal), but that because of the toxicity of the drug it should only be used for those treated in hospital (see also NEUJEAN and EVENS, 1958).

The need for hospitalization when Mel B is used is a very serious disadvantage in the eyes of the British workers, because so much of the treatment must be undertaken in the field: they therefore prefer to give a course of injections of pentamidine and tryparsamide or Antrypol and tryparsamide. Results obtained by the Sleeping Sickness Service of Northern Nigeria have shown that Antrypol-tryparsamide therapy can be expected to result in a cure rate (based on a 2-year follow-up period) of the following order:—

Early cases	about 90%
Intermediate cases	„ 70%
Advanced cases	„ 30%

For late cases, or in areas where tryparsamide resistance is encountered, Melarsen is being used with considerable success (BUTLER, DUGGAN and HUTCHINSON, 1957); resistance to Mel B and Melarsen has been recorded.

It should also be mentioned that in many areas pentamidine only is used for the treatment of early cases of infection.

Prophylactic Treatment

The drug of choice is now pentamidine (lomidine), which has a very considerable prophylactic activity. Although some workers believe that a single injection will protect for one year, the safest regimen probably consists of retreatment at intervals of 6 months. Side effects are not uncommon, but are mild enough to constitute no contra-indication to the extensive use of this drug under field conditions. The subject has been reviewed by GALL (1954).

Mass prophylaxis with pentamidine has been undertaken on a very large scale in the French-African territories, the Belgian Congo, and in Portuguese Angola (DEMARCHI, 1958). Regular prophylaxis can reduce the incidence to less than 0·1%, but unfortunately, after discontinuation, recrudescence or reintroduction of the disease is to be expected within a few years. This method of control has proved successful where methods of mass survey and treatment have been only partly effective and where eradication of tsetse by felling the vegetation is impracticable owing to the extent of the insect habitat.

In Northern Nigeria the relatively high incidence of sleeping sickness among tin mining labourers working in tsetse-infested streams gave rise to concern, more especially since much of the labour was casual and therefore likely to spread the disease; since 1946, such labour has been most successfully protected with pentamidine (HAY, 1958).

It was concluded at the 7th Meeting of the International Scientific Committee for Trypanosomiasis Research, held at Brussels in 1958, that chemoprophylaxis has been successful in reducing considerably the incidence of trypanosomiasis caused by *T. gambiense*. The factors restricting the use of this method are mainly of an administrative, social and economic nature. Experience has shown that success is dependent on the active cooperation of the local population and administrative authorities.

Epidemiology

During the last 40 years, epidemics of Gambian sleeping sickness have been recorded from most territories in the western half of Africa. Before 1925 the disease was most severe in Angola, the Belgian Congo and French Equatorial Africa; the pandemic then appears to have moved westwards from the Congo

basin, becoming most severe in Nigeria in 1928–36, in the Gold Coast (Ghana) in 1932–40, and in Sierra Leone in 1939–42 (Scott, 1957). The cause of such a pandemic is unknown, but it may be associated with a cessation of tribal warfare, leading to population dispersal in search of new farmland and so to increased man-fly contact, together with the rapid dissemination of trypanosome strains made possible by the introduction of motor vehicles and railways.

It is difficult to relate the picture for western Africa with events at the eastern limit of Gambian sleeping sickness. Following on the great 1901 epidemic on the shores of Lake Victoria, a focus has persisted to the present day around the Kavirondo Gulf in south-west Kenya. Morris (1959) describes how the original epidemic spread northwards down the Nile into the West Nile District of Uganda, which borders on the Belgian Congo; here there were two serious outbreaks, one in 1929 and one in 1936. It would appear that there are certain persistent foci, which give rise periodically to localized epidemics (EATRO, 1958).

Valuable epidemiological studies have been made in various territories, notably Gambia (Hutchinson, 1953), Sierra Leone (Hutchinson, 1954), Ghana (Scott, 1957 and 1959, Morris, 1951 and 1952), and Uganda (EATRO, *loc. cit.*); the interested reader should refer to the above papers, because I propose to discuss here only the fundamental epidemiological principles involved.

If cyclical transmission is to take place, *T. gambiense* must reach the salivary glands; the fly cycle takes at least 18 days and is normally completed in only a very small proportion of individuals, as evinced both by the dissection of wild flies and by attempts to infect tsetse in the laboratory. Recently Wijers (1958) has shown with *G. palpalis* that flies which take an infected feed on the first day of life are far more readily infected (7·6%) than those that take such a feed on the second day (1·1%), third day (0·0%), or later (0·0%). He suggests that for *G. palpalis* to have a good chance of becoming infected with metacyclic trypanosomes the following conditions must be fulfilled: (a) the fly must be willing to feed within 24 hours of emergence; (b) its first host must be man; (c) the man must have sleeping sickness; (d) the disease must be in the early stage, with a sufficient number of transmissible trypanosomes in the peripheral blood; (e) the fly must live for at least 18 days to become infective. The odds seem heavily loaded against successful transmission; how then does it take place in the bush, and how do epidemics occur?

For many years the field evidence has indicated that a high incidence of Gambian sleeping sickness is associated with a close intimacy between the tsetse and human populations. But this intimacy must consist of the same individual flies being in close *personal* contact with man; if the fly population consists of ever-changing individuals the contact may still be close, but being *impersonal* the conditions will be unsuitable for a rapid build-up of cases (Nash, 1948a, p. 66).

Certain factors which restrict the movement of the fly population bring about personal man-fly contact. There is geographical isolation, such as a tsetse-infested sacred grove on the edge of a village, or a thicket-choked moat beneath the encircling town-wall; in neither case can the tsetse population wander, because the surrounding country is intensively farmed and shadeless. Another factor may be lack of natural hosts, man in his meat-hunger having destroyed all wild life around his village. But by far the commonest factor in the restriction of fly movement, and one which brings about a seasonal intimacy in man-fly

contact, is adverse climate; the nearer the fly is to the hot dry limits of its range, the more effective is this factor.

In the drier parts of the savannah zone the distribution of *G. palpalis* and *G. tachinoides* becomes seasonally limited to the immediate vicinity of permanent pools of water in the stream-bed, where the microclimate makes survival possible. The villages are also situated near such permanent pools, because man becomes dependent upon the water-holes when his shallow wells have dried up (NASH and PAGE, 1953); under such circumstances a very small tsetse population may be responsible for a very high incidence in man, because of the close personal nature of the man-fly contact. In 1935 I came across a classic example of this when I investigated a certain hamlet which had a 70% infection rate among its 43 inhabitants. Exhaustive search of the dried-up stream-bed failed to produce a single tsetse except at one spot, immediately below the hamlet, where the sand was wet and the villagers had scooped out a shallow hole; here I caught 4 *G. palpalis*. Each woman had to take her turn sitting by the hole: with a curved section of calabash she would collect a cupful of water, then wait for more to seep into the hole, until after about 15 minutes her water pot was full and someone else took her place (NASH, 1944). I doubt if the tsetse population consisted of more than a dozen flies, but one can picture how one of the villagers, who had recently picked up the disease elsewhere, was bitten at the water-hole by a newly emerged fly made avid by the heat; how that fly, restricted in movement by the climatic barrier, lurked by the water-hole, feeding on man at intervals of perhaps 3 days; by the 18th day this fly could have become dangerous and, if a female, could easily live for 60 days.* In this eventuality she *could* transmit 14 infections before she died. Admittedly, this is taking an extreme case in which all factors are assumed to be aiding transmission, but it does show that, given favourable circumstances, the fulfilment of Wijer's 5 conditions would not be difficult.

Occasionally the favourable wet season climate will permit riverine tsetse to take up temporary residence within a village, especially if there are attractive features such as clumps of mango: MORRIS (1959) describes conditions on the River Aswa in Northern Uganda, where some houses are situated within loops of the river, often with riverine vegetation on 3 sides of them, and where *G. palpalis* can be found in or around the houses at almost any time of year.

Having considered the spread of the disease within a village community, let us now turn to the spread from one village to another. All Africans are inveterate market-goers and travellers, and on all routes there are favoured halting places where the path crosses a stream offering a drink to the thirsty, attractive shade to the weary, and a meal to the tsetse; such crossing places, at which the fly concentrate, must be very important in the transmission of the disease. There are also definite focal points within the tsetse's riverine habitat which are much visited by people from adjacent villages, such as reaches of a stream where good roofing poles grow, favoured fishing sites, and forest areas where palm-wine tapping is practised; at such points the man-fly contact is probably less personal than at the village water-hole, but sufficient to spread the disease.

Much wider dissemination of sleeping sickness takes place along the main thoroughfares of a country; SCOTT (1957) has paid particular attention to the

* A female has been recaptured 184 days after marking (NASH and PAGE, 1953).

relationship between such highways and the distribution of human trypanosomiasis in Ashanti, Ghana.

An interesting point is that sleeping sickness is very rare in all but the driest parts of the West African forest belt, even though *G. palpalis* may be present; at last a satisfactory explanation has been found for this puzzling feature in the distribution of the disease. PAGE and MCDONALD (1959), the one working in the humid forest belt in the south of Nigeria and the other in the arid savannah in the north, undertook two similar fly-marking experiments at water-holes. Any fly marked and released at the water-hole which was recaptured at the same place 18 days or longer after marking was considered to be a potential transmitter; in the dry season the proportion of such flies in the north was about 9 times greater, and in the wet season about 7 times greater, than in the south; further, in the north the proportion of such "transmitters" was nearly twice as great in the dry season as in the wet, indicating concentration at the water-holes when the climate was severe. In the humid conditions of the southern locality *G. palpalis* is barely riverine in habit, roving freely throughout the farm land, woodland and forest (PAGE, 1959); consequently the man-fly contact is impersonal, which probably explains the virtual absence of sleeping sickness from this zone.

Even though in the laboratory *T. gambiense* can be transmitted by *G. morsitans* (TAUTE, 1911), the epidemiological evidence suggests that this tsetse plays no part in the transmission of Gambian sleeping sickness. For example, HUTCHINSON (1953) demonstrated in the Gambia the virtual absence of the disease from *morsitans*-infested villages, when it was prevalent a few miles away in villages in contact with *G. palpalis*.

Control Measures

(*a*) *Movement of the Population.* The removal of the human population from the vicinity of the tsetse was the earliest method to be employed for the control of Gambian sleeping sickness. Later, this method became integrated with rural development, as in the Nigerian Anchau Settlement Scheme: having made a tsetse-free corridor, covering 600 square miles of bad sleeping sickness country, the existing population was augmented by the movement into model villages of the people who lived outside in scattered communities; attention was then turned to the improvement of the health, nutrition, agriculture and living standards of the 50,000 inhabitants of the corridor (NASH, 1948b).

(*b*) *Mass Survey and Treatment.* This control measure is based on the conception that since man is the main, if not the only, reservoir of *T. gambiense*, the successful treatment of every case should deprive the fly of its source of infection. The idea of seeking out and treating all infected persons, by repeated examination of the whole population at risk, was first developed by Belgian and French workers (VAN HOOF, 1947; LE ROUZIC and KOCH, 1949); the method was adopted with modifications by all the British West African territories (DAVEY, 1948). (In French and Belgian possessions mass treatment is now giving way to mass prophylaxis with pentamidine.) Two examples will be given to illustrate the scale and effectiveness of this measure.

In French West Africa, between 1932 and the end of 1953, over 401,000 cases of sleeping sickness were discovered. Whereas in 1941, 28,239 new cases

were found among 3,891,299 people examined, in 1953 there were only 6,902 new cases among 5,407,376 people examined (MASSEGUIN and TAILLEFER-GRIMALDI, 1954). The results were obtained without recourse to anti-tsetse measures, and indicate that mass treatment can control but not eradicate the disease.

In Nigeria the system of mass survey and treatment was started at the end of 1930, but after completion of treatment a dispensary would be set up to deal with relapses and fresh infections, thus obviating the necessity for annual resurveys which are very costly and can prove obnoxious to some tribes; the dispensary staffs would undertake frequent village surveys throughout their areas in order to bring in the early and relapsed cases. The policy also included anti-tsetse clearings aimed at breaking man-fly contact wherever possible, as it was felt that although slow in application this measure provided the only hope of consolidating the position won by chemotherapy (LESTER, 1945; MCLETCHIE, 1948). Between 1931 and 1952 over 556,000 persons were treated, the great majority in Northern Nigeria.

The following table illustrates the effectiveness of the measures described (see MCLETCHIE, 1953):—

Year	No. Examined	Infection Rate %
	New Surveys	
1931–1940	2,756,343	10·9
1946–1952	473,831	0·3
	Team Re-surveys	
1944	114,746	2·0
1951–1952	672,692	0·2
1955	Annual	0·21
1956	Average	0·15
1957	about	0·15
1958	1,750,000	0·14

Whereas in 1935 the total number of patients treated was nearly 90,000, the number now is around 5,000 per annum, and therein lies the danger: the importance of a disease which produces annually a mere 5,000 cases among a population of nearly 17 million is liable to be underestimated, but many of the foci remain, and if the present excellent control measures are given up in Northern Nigeria, or elsewhere, the conditions of the thirties will soon be seen again.

It is generally accepted that treatment alone is unable to eradicate the disease; it can stop the spread of the infection, but seems unable to eradicate it from the old endemic foci; in places where the infection rate flares up to 2–5% every few years, the tsetse population should be eliminated if possible.

(*c*) *Vector Control by Clearing Vegetation.* The temperature and humidity requirements of *G. palpalis* and *G. tachinoides* are such that they can only survive the dry season climate of the woodland savannah zone by adopting a linear distribution along the watercourses, where they take advantage of the microclimates.

Man cannot alter the general climate, but he can destroy a microclimate which is kept in being by the insulating effect of riverine vegetation; by felling such vegetation, or modifying it sufficiently to permit the entry of the hot dry

wind from the savannah, the microclimate can be altered and these tsetse destroyed (NASH, 1940); this is the basic principle upon which the clearing technique, used against waterside tsetse, depends. As the main forest belt is approached, the rainfall becomes higher and the fringing forest more extensive, until a stage is reached where both the initial clearing cost and the speed of regeneration make this measure economically impracticable.

If all the riverine vegetation is felled, the clearing is described as "ruthless"; if only the undergrowth and low-branching trees are removed, the clearing is referred to as "partial". For the last 22 years partial clearing has been employed in Nigeria; but at the point where a stream system leaves the populated area, a mile-long ruthless barrier clearing is made to prevent wet season invasion from the uncleared end, as in the rains tsetse could survive in partial clearing if allowed access (NASH, 1948a). The method is effective and tsetse have been eradicated from hundreds of miles of stream, with benefit not only to man, but also to his cattle; for instance, in one area in Northern Nigeria over 3,000 miles of stream were cleared between 1950 and 1957 (NORTHERN NIGERIA, 1958).

A cheaper method, known as "protective" clearing, is to clear ruthlessly only those parts of the stream in the immediate vicinity of villages and important crossing-places. MCLETCHIE (1948) gives a good example of the value of protective clearing: the re-survey of 3 neighbouring areas, where no dispensary treatment had been available, gave infection rates of 2·8, 0·9 and 0·1%; in the first area there had been no protective clearing, in the second unorthodox clearing, and in the third efficient clearing.

In Ghana, MORRIS (1946) and his successors have also eradicated riverine tsetse from large areas of country; Morris approached the problem from a different angle, but the final appearance of his clearings was very similar to those undertaken in Nigeria (BUXTON, 1955).

(*d*) *Vector Control with Insecticides.* Increase in clearing costs due to rising wages has focused attention on insecticides, whose application needs much less labour. The insecticidal approach has the potential disadvantage that it does not alter the tsetse's habitat, so that given access the fly could readily become re-established. Since riverine tsetse can wander through the woodland in the rains, and be carried some miles by man, motor vehicles or game, they could gain access, even across a watershed, into a system whose tsetse had been destroyed by spraying; only experience will show how great is this danger.

In Kenya, *G. palpalis fuscipes* has been exterminated from more than 300 miles of the Kuja-Migori river systems (GLOVER, LE ROUX and PARKER, 1958); the results have been achieved by a combination of spraying with insecticides and the creation of cleared barriers to prevent re-infestation. Including bush clearing, insecticides, vehicles and wages, the cost was £120 per river mile, whereas the average cost of the barrier clearings was £150, rising to £200-£300 in denser areas. Shoulder sprayers were used along narrow paths cut on both banks close to the water's edge, but if the width of the vegetation exceeded 60 yards, further paths had to be cut at 60-yard intervals; the final technique consisted of spraying 3 times, at intervals of 3 weeks, with Dieldrix 15 diluted to 1·8% with water; if re-infestation occurred after the third application, a "knock-out" dose of 5% Dieldrix was administered. The measure has resulted in a spectacular reduction in the number of cases of sleeping sickness.

In the dry Sudan savannah zone of Nigeria, insecticidal methods for the

control of *G. tachinoides* are now standard practice: eradication can be achieved by a single application during the dry season of 5% active DDT, which is usually applied as a suspension in water. A recent project involved 482 miles of river system, of which 394 miles were sprayed and 88 miles cleared to produce barrier zones between sprayed blocks. The cost averaged £14 per mile, which included the barriers (at 60% of the whole), 77 miles of track fit for motor vehicles, insecticides and local labour. In the more humid Guinea savannah zone, where *G. palpalis* is dominant, DDT applied as a wettable powder has not been successful even after repeated applications; however, a single application of 4% Dieldrin emulsion appears to be remarkably effective, even when applied in the wet season; it seems probable that Dieldrin at a lower concentration would still be effective (personal communication from Mr. R. J. KERNAGHAN, Senior Entomologist, Ministry of Health, Northern Nigeria, 1/12/59).

(*e*) *Effectiveness of Control Measures.* VAN OYE (1958) has collected the annual sleeping sickness returns for each country from 1948 to 1957, and has produced tables giving the yearly total of new cases and the infection rate expressed as new cases per 10,000 inhabitants. Since in some countries, such as Northern Nigeria, several millions of the population are never at risk, and since many years may elapse between each census, the writer prefers to consider the annual number of new cases: Van Oye's figures for all countries combined show that the number of new cases of *T. gambiense* infection have fallen *steadily* from 53,408 in 1948 to 14,874 in 1957; clearly the control measures employed are effective.

Rhodesian Sleeping Sickness

The course of normal *rhodesiense* infection has already been briefly described. In its typical form, the untreated disease progresses rapidly to death within some 3–9 months (WILLETT, 1955). DYE (1927) states that it is well known in Tanganyika Territory that trypanosomes may be present in the blood for some time before symptoms appear, and instances such a case, the patient, during a month's observation, remaining in the most robust health. ROSS and BLAIR (1956) describe cases of "carriers" who had trypanosomes in the blood for some months but remained in perfect health; they also quote instances from Southern Rhodesia in which the onset of the disease must have been very slow, as these persons, who had come from tsetse country, were known to have been working on European farms in completely fly-free surroundings for periods as long as 29 months before falling ill. Such "carriers" may play an important part in the epidemiology of a normally acute disease, but as they are without symptoms, there is understandably little knowledge as to the frequency with which they occur.

As mentioned earlier, Rhodesian sleeping sickness is essentially a disease of the sparsely populated woodlands and the number of cases treated annually is small compared with the Gambian disease. BUXTON (1948), when summing up the importance of sleeping sickness in eastern Africa (not all of it of the Rhodesian type) concluded that in the absence of an epidemic, Kenya, Uganda and Tanganyika together notify less than 2,000 cases per annum, and that Northern and Southern Rhodesia, Nyasaland and Ngamiland provide about 100 cases per annum. In Tanganyika Territory, in 25 years, 1922–46, the total number of cases of *T. rhodesiense* infection diagnosed was nearly 24,000

(FAIRBAIRN, 1948); for the last 3 years, 1956–58, the figures are 646, 411 and 555 respectively. In the 14 years, 1942–55, the total number of cases for Northern Rhodesia was 784, and for Southern Rhodesia, 111 (MORRIS, 1956).

Such figures seem trifling, but it is the potential of the disease that is so alarming. The chief vector, *G. morsitans*, does not have a linear distribution, but occupies thousands of square miles of woodland where conditions appear to be suitable for the transmission of the infection; already the disease has spread into many new areas, as can be seen from Fairbairn's map (FAIRBAIRN, *loc. cit.*). When one remembers that the results of the Tinde experiment showed that *T. rhodesiense* can be maintained in animals for 23 years without losing its infectivity to man, one appreciates the absolute necessity for continuing the present vigilance and controlling each local outbreak before it has time to assume epidemic proportions and spread.

Diagnosis

Diagnosis is normally undertaken by examination of blood films only: trypanosomes are usually more numerous in the blood, and cervical glandular enlargement is a less typical feature, than in the Gambian form of the disease. Lumbar puncture is employed in doubtful cases.

Curative Treatment

Suramin BP (Antrypol, Moranyl, Bayer 205) is the most commonly used curative drug for the treatment of early cases of *T. rhodesiense* sleeping sickness. Pentamidine is considered to be less active, and Mel B too toxic for use in routine treatment; in advanced cases, however, Mel B is used (conclusion reached at the 6th Meeting of the International Scientific Committee for Trypanosomiasis Research [ISCTR], 1956). An appraisal of trypanocidal drugs, as found in Mozambique, has been made by DE ANDRADE SILVA (1956).

Mel B is undoubtedly a most valuable drug for use in advanced cases which would otherwise be incurable; even a few almost moribund patients have been brought to a state of probable cure (APTED, 1957b). Cases of Mel B resistance have been recorded.

Prophylactic Treatment

Although mass chemoprophylaxis with pentamidine may sometimes be of value in controlling an epidemic, normally the method is neither practicable nor economic because the incidence of the disease tends to be very low and to occur in widely scattered populations (conclusion reached at the 7th Meeting, ISCTR, 1958). It should be noted that DE ANDRADE SILVA and CASEIRO (1956) found pentamidine prophylaxis valuable in controlling an epidemic in Mozambique.

Epidemiology

In East Africa, as in West, the introduction of a peaceful administration led to the disintegration of many of the old settlements; parties, sometimes consisting of only a man and his family, would go off to bush and set up small, remote habitations of their own: instead of being insulated from the woodland tsetse by extensive cultivation, people now started to live in close contact with the

fly. To these, and other factors, MACLEAN (1929) attributes the increase in sleeping sickness which started after the 1914–18 war.

The epidemiology of Rhodesian sleeping sickness is complicated by the presence of an animal reservoir; it will be better understood when we know which species are the important carriers under field conditions.

Indications as to the reservoir-potential of certain members of the fauna have been obtained by studying the course of the disease in captive animals which have been infected with *T. rhodesiense*, transmitted usually by a single *G. morsitans*. The work on this subject, mainly undertaken in Tanganyika Territory over the past 18 years, has recently been summarized (ASHCROFT, BURTT and FAIRBAIRN, 1959). Some species, such as Thomson's gazelle, are highly susceptible to infection and usually killed by it, the blood typically being positive until death; they are rarely fed on by tsetse in the field. Some species, such as the common duiker, eland, reed-buck, spotted hyena, oribi, bush-buck, and impala are tolerant, nearly always become infected, and have blood-positive periods of considerable duration. Other species, such as the wart-hog and bush-pig, usually become infected but are more resistant, the parasitaemia being scanty and typically not persisting for long. It is the second group, to which more species may be added on testing, that the potential reservoirs are likely to be found.

The writer suggests that the important carriers may consist of only two or three species whose habits are such as to produce close, personal, beast-fly contact, individual beasts being fed off mainly by the same individual tsetse: in his experience the bush-buck is such a species; although widely distributed, it is localized in habit, several individuals being based on a thicket or stream-bed into which they will bolt at the slightest alarm; such habits enable them to survive near villages, and supply the local tsetse population with a dependable source of food. A family of bush-buck, once infected with *T. rhodesiense*, might produce a localized source of infected flies, and if their thicket was near a hamlet, or in uninhabited country but adjacent to a focal point periodically visited by Africans for fishing, camping, etc., that point could act as an endemic focus of the disease. By way of contrast, the roan antelope is a species which avoids man, roams extensively through the woodland, and runs for miles if alarmed: with the roan, fly contact must be impersonal, so that if a beast ever became infected with *T. rhodesiense* it might infect the occasional fly within a large area of uninhabited bush, but not a number of flies at a focal point.

There is considerable epidemiological evidence that in certain areas game acts as a reservoir of the disease. FAIRBAIRN (1948) gives among other examples the River Ugalla, which was depopulated in 1925–26 and is uninhabited during 6 months of the rains, yet as soon as the fishermen return to the pools, cases of sleeping sickness occur; similarly, cases arise among the people of Kibondo District when they visit, illegally, the salt deposits of Kimyora for 2 to 3 months at the end of each dry season: since the average span of life for *G. morsitans* is not believed to exceed 2 months, it would be impossible for infected flies to survive the periods when these two areas are uninhabited. JACKSON (1955) describes how a total of 27 members of his African staff became infected, while engaged in tsetse research, in 3 different places closed to settlement on account of sleeping sickness.

FAIRBAIRN (*loc. cit.*) concludes that the introduction of the disease into an area can usually be traced to the arrival of an infected human being, and that thereafter the game become infected and then act as reservoirs which maintain it endemically.

DYE (1927) describes an outbreak in Tanganyika Territory among small communities, ranging from about 10 to 200 people, scattered through *morsitans*-infested woodland; his evidence suggests that the disease was transmitted by fly from man to man, and that in this area there was no game reservoir. He points out that even though everyone had to traverse the fly bush when going from village to village, yet the distribution of cases was largely confined to certain of those hamlets in which the farm-clearing was so inadequate that the tsetse *lived* among the huts; in some such hamlets the people remained healthy indefinitely, but in those in whom cases occurred he could trace the start of the disease to the arrival of an infected visitor. He also demonstrated how localized was the spread of the infection among huts, and how in one village, made up of widely scattered communes, all 3 cases were in the same commune. (His results strongly suggest that there must have been personal man-fly contact, the same individual *G. morsitans* remaining long enough in the vicinity to transmit the disease from person to person.)

Dye's most convincing evidence that there was no game reservoir in this area was provided by the population of the most heavily infected village, which had been evacuated to a fly-free zone; after 2 months of observation, the healthy persons were allowed back to their village which had meanwhile been over-run by game: they spent 2½ months there, before returning to their new settlement, but none developed the sickness during the next 20 months of observation. Had there been a local game reservoir, one would have expected new cases to develop, but as none did, it seems reasonable to suppose that the removal of the human source of infection for 2 months permitted the infected flies to die out. (Possibly the species of game which act as reservoirs were absent from this area?)

FAIRBAIRN (1948) has shown that the proportion of infection in women and children is higher when epidemic conditions prevail and fly enter the huts, than it is in the well-established settlements where the great majority of cases occur among men who journey into bush in search of forest produce.

It is known that the incidence of Rhodesian sleeping sickness is greatest in the hottest months of the year, and that under laboratory conditions much higher transmission rates can be achieved from *G. morsitans* which have emerged from pupae incubated at 30°C. The increase in the number of cases noted in the hot dry season is probably due to the combined effects of occupation leading men into the fly bush and of high temperatures increasing the proportion of infected flies (FAIRBAIRN, *loc. cit.*).

I will now mention certain points which Dr. F. I. C. Apted, Sleeping Sickness Service Specialist, Tanganyika Territory, has kindly brought to my attention. The truth is that there are great gaps in our understanding of the epidemiology. Why do certain districts, which are apparently suitable and in contact with adjoining sleeping sickness areas, remain free of the disease for years, and then suddenly produce explosive outbreaks? Conversely, why does the disease tend to die out in one area, at a time when the cycle of incidence is rising throughout the territory? (Is this due to a local build up of immunity, or to a decrease in the pathogenicity of the local strain of trypanosome?) The

disease undoubtedly waxes and wanes over the years, as judged by the total cases treated; the reason is unknown, but is probably associated with climatic variations which affect the size of the fly population, the infectibility of the tsetse, and the habits of the people. Clearly, there is much that is not understood.

Finally, mention must be made of a recent outbreak of sleeping sickness in south-east Uganda where *T. gambiense* has been completely replaced by *T. rhodesiense*, possibly since an epidemic in 1940; the major vector appears to be *G. pallidipes* (ROBERTSON and BAKER, 1958). The epidemiology has been studied, but will not be referred to as it is quite atypical of that usually associated with Rhodesian sleeping sickness.

Attention must be drawn to an interesting review of the epidemiology of trypanosomiasis by ASHCROFT (1959c), which was published too late to be considered in this paper.

Control Measures

(*a*) *Mass Survey and Treatment.* Experience has shown that with Rhodesian sleeping sickness treatment alone can never control an epidemic and is merely a palliative (FAIRBAIRN, 1948); its ineffectiveness may be due to the infection persisting in animals.

(*b*) *Movement of the Population.* The value of settlement as a means of controlling the disease, its widespread use and the sociological and agricultural implications, have been fully discussed by BUXTON (1955); the following details on the application of the measure in Tanganyika Territory have been culled from FAIRBAIRN (1943 and 1948).

Observation has shown that the condition most favourable to an epidemic is a low density of 16–18 people per square mile, whereas, with a density of 100 or more, many villages are large enough to protect themselves from tsetse by the clearings made for their farms. The policy, started by MACLEAN in 1922, was to break man-fly contact by concentrating the population of scattered hamlets into settlements holding 2,600 to 3,500 people, the larger figure being preferable. The new settlements usually had to be sited within the tsetse-infested woodland because the people would have refused to leave their tribal lands; owing to the time it took for them to clear sufficient bush to affect the tsetse, it was 2 to 4 years before the incidence fell. Between 1922 and 1945 nearly 140,000 people were removed from isolated hamlets, producing a marked influence on the total number of cases treated in the Territory; for example, the number of cases diagnosed during 1929–32 was 9,329, but during 1939–42 only 2,647. The people had no cattle at first, but once the tsetse were pushed back, large numbers of stock were successfully kept, indicating how fly-free the country became in the vicinity of these large settlements.

(*c*) *Vector Control by Clearing Vegetation.* The earliest clearing method consisted in felling all the woodland and thicket, which is difficult in thinly populated areas. However, with a greater knowledge of tsetse ecology, the technique of " discriminative " clearing was introduced, which virtually implies the clearing of only those parts of the bush which form the essential tsetse habitat; the bush which has to be cleared varies in different areas according to the type of vegetation and the species of tsetse (FORD, 1954). The work at Abercorn, Northern Rhodesia, affords a good example: concentrations of

G. morsitans were found in certain of the shallow valleys forming the headwaters of small tributary streams; several of these were cleared of vegetation with the result that the density of *G. morsitans* was at once depressed, not only in the valleys themselves but over wide areas of untouched woodland. The method was extended with great success to cover an area of 280 square miles, of which only 3% had to be cleared (GLOVER, JACKSON, ROBERTSON and THOMSON, 1955).

Discriminative clearing has been successful in many areas, but not always: the failures may be due to faulty appreciation of the extent of the essential tsetse habitat, the extent varying from place to place according to the severity of the climate and other factors.

FAIRBAIRN (1948) concluded that the soundest control measure would appear to be the settlement of the people in open country, which had been enlarged to receive them, combined with discriminative clearing in the adjacent woodland, so that firewood, thatching grass, etc., could be collected in safety. As a result of improved techniques, the current policy favoured by Apted in Tanganyika is to open up and develop the country by discriminative clearing, rather than to retreat from the fly behind settlement boundaries, but the old settlements are maintained (APTED, 1957a).

(*d*) *Vector Control with Insecticides.* For the control of Rhodesian sleeping sickness, the use of insecticides against *G. morsitans* and *G. swynnertoni* is likely to be impracticable, as the fly belts are normally too vast; insecticides may, in favourable circumstances, be of value when *G. pallidipes* is the vector.

(*e*) *Effectiveness of Control Measures.* The annual totals of new cases of *T. rhodesiense* infection for all countries combined, as given by VAN OYE (1958) for the 10 years 1948–57, show no steady decrease, as was the case with his figures for Gambian sleeping sickness; on the contrary, the totals fluctuate at a low level: for example, there were 1,089 new cases in 1948 and 1,240 in 1957, with only 854 cases in 1952, but 2,066 in 1954. It would seem that the measures employed suffice to keep the disease under control, but are incapable of reducing the incidence still further, possibly because they are only effective against the human reservoir, and leave the game reservoir untouched.

Animal Trypanosomiasis or Nagana

Since nagana is only of indirect medical interest, the subject will be dealt with less thoroughly than its importance deserves. Animal trypanosomiases form a group of allied diseases (HORNBY, 1952), but here we are only concerned with nagana in cattle which will be referred to as a single disease, since control measures do not vary with the causal organism.

Diagnosis

In a well-fed herd of cattle, the "fly-struck" ox, even though eating fairly well and ruminating and dunging normally, is conspicuous by its thinness, loss of strength and condition; in an under-nourished herd the difference is not recognizable by the ordinary observer (HORNBY, *loc. cit.*). Diagnosis is normally undertaken by examination of blood films.

Curative Treatment

There are good curative drugs such as Ethidium bromide, Antrycide methylsulphate, Berenil and Prothidium, but, in areas where there has been much

treatment of cattle in the presence of fly, treatment has become bedevilled by the appearance of resistant and cross-resistant strains of trypanosomes; of the new agents, Metamidium chloride shows the highest degree of curative and prophylactic activity against strains which exhibit resistance to the older drugs.

Prophylactic Treatment

In 1950, prophylaxis became possible with the introduction of Antrycide Prosalt; the duration of protection achieved varies according to the density and infection rate of the local tsetse, which is known as the "challenge". Under conditions of medium challenge, Prosalt is administered at intervals of two months.

More recent drugs, with promise of considerably greater prophylactic activity, are in the process of testing in the field; results from different areas are often conflicting, which is usually due to variations in the severity of the local challenge, but can, in an old testing site, be due to the degree of drug resistance or cross-resistance present in the local strains of trypanosomes.

It now seems clear that to reduce the risk of drug resistance arising in the field, one should first ascertain by a pilot experiment the minimal period of protection afforded by the drug of choice, reduce this period for safety by about one quarter, and thereafter adhere rigidly to the indicated regimen for re-treatment. A "stopper" drug, known to be effective against strains resistant to the drug of choice, should be kept in reserve.

For recent reviews on the chemotherapy and chemoprophylaxis of animal trypanosomiasis, the reader should consult DAVEY (1957) and MARSHALL (1958).

Epidemiology

The great difference in the epidemiology of human and animal trypanosomiasis is that in many areas man, unlike cattle, can live in the presence of tsetse without contracting trypanosomiasis. Admittedly, there are localities where cattle survive with probably only an occasional death attributable to the disease, but more often the problem is serious, and frequently trypanosomiasis prevents the keeping of livestock; the local situation varies according to the degree of challenge and the resistance to infection of the local breed of cattle.

The severity of challenge will depend partly upon the virulence to cattle of the local strains of trypanosome, and the local abundance of trypanosomes will depend upon the number of hosts present belonging to tolerant species of the fauna. The incidence of infection in the fly will depend upon the infectibility of the tsetse species present, and upon whether or not its preferred host forms a good trypanosome reservoir. The number of bites that an ox will receive per day will depend, among other factors, upon the density of the fly population (which will itself depend upon climate, vegetation and food supply), and upon whether the local tsetse's habitat is linear, in which case the ox will only be at risk when watering, or ubiquitous, when the ox will be attacked throughout the hours of daylight. The subject of "challenge" is complex.

The epidemiology of nagana is ill-defined because it is not normally associated with focal points in the sense described for sleeping sickness.

Immunology

Dwarf breeds of cattle, with considerable resistance to nagana, are widely distributed in West Africa and may even be found in *morsitans* belts, but under these circumstances the writer suspects that the challenge is very low; unfortunately dwarf cattle are of slow growth. It is not yet known for certain whether these cattle have a congenital resistance to trypanosomiasis, or whether they have become infected early in life and developed premunition, that is to say a state of chronic infection without clinical effects (BUXTON, 1955); the evidence suggests that they have developed premunition. The picture should be much clearer in a year or two, when certain existing lines of research have reached fruition.

CHANDLER (1952), working in Northern Nigeria, has shown that the severity of challenge in an area may to a considerable extent be offset by the resistance to infection of the breed of cattle. During 11 months of natural exposure to *G. palpalis* and *G. tachinoides*, all 12 of a herd of Zebu cattle had been positive and 9 had died, but of 8 dwarf N'dama breed only 4 had shown a very transitory low-grade infection and all 8 were alive. In a similar experiment in a *morsitans* belt where the challenge was more severe, the Zebu were all dead in 3 months, but after 6 months all 5 N'dama were well, never having shown positive. In each experiment a herd of N'dama-Zebu hybrids yielded results intermediate between those found for the two thoroughbred herds. Unfortunately under conditions of still heavier challenge, N'dama can die of trypanosomiasis.

Temporary immunity to a high intensity of infection can be induced by preliminary prophylactic treatment with Antrycide Prosalt, administered in a tsetse area (SOLTYS, 1955). This phenomenon is not due to the prophylactic effect of several Prosalt depots, as it has now been shown that after using only curative drugs, in a 7-month immunizing régime under high fly challenge, an immunity is induced of 5 to 12 months' duration; this immunity is probably an antibody response to alternate infection and cure (WHITESIDE, 1958).

Control Measures

(*a*) *Treatment*. It is usually cheaper to use drugs to kill the trypanosome than to employ measures to kill the tsetse, but chemotherapy alone achieves nothing permanent; under conditions of low challenge the land can be used, but it is not reclaimed from the tsetse fly, and is not essentially improved. Chemotherapy is therefore best employed in conjunction with other measures (WHITESIDE, 1958). In Kenya, where drugs have been used with commendable discretion, they have been employed for the following purposes, among others:—

(i) To permit of permanent or temporary ranching in fly-belts, sometimes aided by discriminative clearing to lower challenge.
(ii) To control trypanosomiasis on the fly-infested margins of reclamation schemes.
(iii) To maintain stock in the face of a fly advance, while the necessary clearing operations are undertaken.
(iv) To protect animals passing through fly-belts.

With the introduction of more efficient drugs and a better understanding of how they should be employed, it is no longer essential to achieve tsetse

eradication; if the fly population is greatly reduced, which is far easier and cheaper than eradication, and if adequate steps are taken to guard against drug resistance, cattle can now be successfully maintained in many areas which were formerly denied to them. This marks a great advance in the control of nagana.

(*b*) *Vector Control by Clearing Vegetation.* In East Africa it is often possible to cut off a great block of woodland from the main fly-belt by taking advantage of almost tsetse-free and treeless grass plains; these are linked together by ruthless clearings, making a barrier around the block, which can then be reclaimed by discriminative clearing or other methods. Unfortunately in West Africa there are no such grass plains; the *morsitans* woodland extends interminably, which makes isolation prohibitively expensive: a barrier usually has to be 2 miles wide and may be many miles in length.

A major problem is to halt advances by *G. morsitans*. The old method was to make a ruthless barrier clearing some miles ahead of the supposed "front line", but often the barrier was not completed in time. A technique employed with success in Tanganyika is "defence in depth": discriminative clearing is undertaken within a belt 4 or 5 miles deep, across the front of the advance; to prevent game carrying flies across, a fence may have to be erected. For examples of the schemes undertaken by a tsetse reclamation department, see LLOYD (1959); the costs given for discriminative clearing against *G. swynnertoni* and *G. morsitans* range from 7 to 11 shillings an acre, but when spread over the total area reclaimed may be as low as one shilling.

Under certain circumstances mechanical means have been successfully used for clearing, but usually hand-labour is cheaper. Phytocides are selective in action and very expensive: in Mozambique, ESTEVES DE SOUSA (1958) obtained about 75% of probable kills, his inclusive costs equating to about £7 an acre when treating foliage, and over £5 when treating stumps; his tests were on vegetation which regenerates so rapidly that *G. austeni* can become re-established within 2 or 3 years of clearing.

(*c*) *Vector Control with Insecticides.* Much fundamental research has been carried out on this subject by the Colonial Pesticides Research Unit in Tanganyika Territory. Insecticides are of undoubted value in eradicating riverine tsetse which have a linear distribution; they are also of value in destroying *G. pallidipes* whose dependence on thicket for breeding permits the attack to be concentrated on the restricted area of the true habitat.

The most ambitious project to be successfully undertaken with insecticides was the eradication of *G. pallidipes* from Zululand, which took 7 years to achieve. In 1945 there was an exceptionally severe epizootic of nagana among cattle on European farms and in herds belonging to Africans around the game reserves. Pupal surveys revealed that the breeding areas and permanent haunts, from which the fly dispersed at favourable seasons, occupied only 200 square miles out of 7,000 square miles of seasonal fly-belts, *i.e.*, less than 3%. The breeding areas were treated from the air with at least 8 applications of DDT or BHC smoke (produced from the hot exhaust of the aircraft engine), or from the ground, in certain mountainous or rugged localities, by using DDT smoke generators or discriminative clearing; in the fly dispersal areas, which were too vast for aerial application, the cattle were dipped weekly in DDT emulsion. The cost of the operation was heavy, working out at 9 to 10 shillings per acre for the 7,000 square miles which were rendered fly-free, but in the

light of the experience gained Du Toit (1954) believes that the figure could have been reduced to less than 2 shillings; however, the Zululand belt was naturally isolated, being 450 miles from the main fly-belts to the north, otherwise the costs would have been far higher.

The economics of reclaiming fly-country must be related to the stock-holding capacity of the land, which in much of Africa is very low owing to annual grass fires and a prolonged dry season. For the purpose of eradicating *G. morsitans* from the vast areas of woodland, it seems that the cost of insecticidal attack, including isolation, is likely to be prohibitive, and the method normally too speculative, because of the risk of the work being nullified by fly becoming re-established in an unaltered environment. In exceptional circumstances, however, the use of insecticides for the control of this tsetse may be practicable. Near the extreme northern limit of its range in Nigeria, the distribution of *G. morsitans* is restricted to linear strips of riverine flood plain, and in the late dry season is still further restricted to evergreen forest islands. By hand-spraying 200 acres of such forest with DDT, *G. morsitans* has been eradicated from 7 square miles of flood plain; the cost of insecticide and application was £700, or about 3 shillings per acre of plain reclaimed, but owing to natural isolation no barriers were needed (MacLennan and Kirkby, 1958).

(*d*) *Vector Control by Destruction of Game.* This method is naturally viewed with dislike by everyone, including those who have reluctantly been forced to employ it in the interest of the cattle and the economy of the country. As is always the case where sentiment is involved, there has been much ill-informed criticism by people lacking practical experience; the subject has been very fairly reviewed by Buxton (1955).

When the game tsetse (*G. morsitans, pallidipes* and *swynnertoni*) advance on an extended front, the herds are decimated, the land is abandoned, and there is a clamour for action. When the problem is urgent and on a vast scale, game destruction is undoubtedly a cheap method which will halt an advance and enable the fly to be pushed back. Discriminative clearing is usually effective and wherever possible should be used in preference to game elimination, but it takes time to ascertain the components of the vegetation which must be cleared, and if these are extensive the population may be insufficient to undertake the work.

In Southern Rhodesia *G. morsitans* disappeared from huge tracts of country at the time of the great rinderpest epizootic of 1896, but by 1924 tsetse were re-occupying large areas, and a policy of game elimination was started. By 1956 many fly advances had been halted, and 10,000 square miles of country reclaimed from the tsetse (Chorley, 1956); the cost worked out at about 6 pence per acre (Buxton, 1955). As Buxton points out, owing to the very sparse human population of Southern Rhodesia, it is unlikely that any other method would have been as successful, but in places clearance of scrub should have been more generally employed. The present policy is to use game eradication only when strictly necessary to supplement and accelerate other measures; as a result, 26,465 fewer animals were destroyed in 1958 than in 1954–55 (from report of Director of Tsetse and Trypanosomiasis Control and Reclamation for year ended 30th September, 1958).

Game destruction has been used as a means of tsetse control in many countries, but its use in Uganda has been singularly well documented. In the

1920s the reduction in elephant numbers in central Uganda, and the introduction of an agricultural policy of early grass-burning to prevent erosion, encouraged the densification of bush, converting fly-free, open grazing country into potential tsetse habitat; after the next wave of fly advances started in the late 1930s, nearly 8,000 square miles of cattle country were lost to *G. morsitans* and *G. pallidipes*. So grave was the position that the very existence of the cattle industry in the Protectorate was threatened. A policy of game elimination, combined with fierce, late dry season burning to reverse the process of bush thickening, was started about 1945, and by 1958 some 6,000 square miles of land had been won back and most of it re-occupied by cattle; 58,000 wild animals had been killed. The cost of the field work was only 7 pence per acre, but, if all administrative overhead expenses, transport etc. are added, the figure rises to about 2 shillings. (Bush felling of the *G. pallidipes* habitat would have cost up to 60 shillings per acre.) Between 1945 and 1956 the cattle population of Uganda increased by 800,000 animals worth about £10,000,000. By using discriminative clearing 1,700 square miles were successfully reclaimed in Karamoja, but in Ankole the method failed to hold the tsetse after 6 years of effort costing at least £140,000 (ROBERTSON and BERNACCA, 1958; RANDALL, 1959).

There would seem to be occasions when a policy of game destruction is justified, but it must be admitted that ignorance of the food preferences of the different species of tsetse *may* have led to the unnecessary slaughter of many species of the fauna. We are still at the stage of ascertaining the most favoured hosts, and do not yet know whether the selective slaughter of only the most favoured species will lead to the eradication of the tsetse, or whether the fly will merely transfer its attention to hosts that are normally rarely attacked. I suspect that if the fly is deprived of its first choice, it may perforce utilize its second or even third choice, but that if these are destroyed the tsetse will cease to flourish. I suggest that "preference" may be a combination of true preference and host availability: to date, the known favoured hosts—pig, bush-buck and rhinoceros—are all species which tend to be found in the same locality day after day, making them far more available to a local tsetse community than transitory herds which are here today and gone tomorrow. Destruction of the readily available hosts should lead to an increase in fly activity and a more rapid exhaustion of reserves of fat and water, which could be serious in the hot season.

Conclusion

In reviewing the subject of African trypanosomiasis, I have attempted to present it as a fascinating biological complex. Even in these days of unavoidable specialization, a strictly medical, entomological or veterinary approach to the problem would be retrograde, as it is hoped that this review will have made abundantly clear.

Examples of the epidemiology and various control measures used against Gambian and Rhodesian sleeping sickness have been taken mainly from Nigeria and Tanganyika Territory respectively, because these two countries have furnished the majority of cases found in the British territories; the British territories have been selected because the British have undoubtedly been the main contributors to the study of the vector, thus permitting a biological

approach to the subject. However, it would be a great mistake for the reader to receive the impression that the British are the only people to have done any work on the problem. The French and Belgians have been the pioneers in mass treatment, both therapeutic and prophylactic, and the Portuguese are undertaking magnificent work in controlling both the disease and the vector.

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SUMMARY OF RECENT ABSTRACTS *

VIII. TYPHUS GROUP OF FEVERS †

General

WEYER (p. 1015) has published a review of the rickettsial diseases of man. They are widespread in the Cameroons, and GAMET and MARTIN (p. 1016) state that in Yaoundé they now account for 30% of hospital cases; the clinical appearances may resemble those of several other diseases, and a rickettsia agglutination test is therefore important in diagnosis.

ROGER and ROGER (p. 141) describe a simple modification of Wright's stain for rickettsiae and the psittacosis-lymphogranuloma viruses, and YAMAMOTO *et al.* (p. 603) describe a method for the purification of suspensions of various rickettsiae.

Experimental work suggests that simultaneous injection of rickettsiae and chlortetracycline is a more reliable method of producing asymptomatic infection —and immunity—than by inoculating living rickettsiae and giving repeated doses of the drug afterwards (KEKCHEEVA, p. 814).

Proteus OX19 Type. Vectors: Louse and Flea

The first case of Brill-Zinsser disease to be recognized in the Netherlands is reported by MINKENHOFF and GISPEN (p. 142), and MISKOV (p. 1120) reports the disease from Yugoslavia.

Louse typhus occurred extensively in Poland during the war of 1939–45, but incidence fell off rapidly afterwards; LUTYNSKI (p. 706) comments on cases observed between 1950 and 1955, concluding that most were relapses resulting from previous infections, but that some were new. Positive complement-fixation tests for typhus have been found in quite a high proportion of Polish refugees in Britain, and LAWY *et al.* (p. 25) therefore comment that any patient from Eastern Europe who has a history of typhus should be examined for specific antibodies as a possible case of Brill-Zinsser disease. ZIVKOVIC and SIMIC (p. 707) show that complement-fixing antibodies to *R. prowazeki* may be found at high titres in about 80% of patients for 12 years after the attack. This persistence suggests a carrier state which may become activated into relapses and give rise to epidemics. In a discussion of typhus in the U.S.S.R. SOMOVA *et al.* (p. 1119) remark that in recent years more than half the patients had had a previous attack or had been exposed to the risk of infection.

LEGKODIMOVA (p. 1118) reports that the typhus observed in the Primor'e region of Eastern Siberia in 1954–6 was due to *R. prowazeki*; recurrences are common but louse infestation is negligible. MARIEV and KUZ'MINA (p. 601) report on 112 patients with typhus observed in Stalingrad, remarking that half of them had had it before, and most of the patients were over 40 years old; it seems probable that for the most part it was the relapsing form of the disease.

Investigation of sources of infection in cases of louse typhus in Russia suggested to PASTUKHOVA (p. 706) that recurrence of the disease is usually due to

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1959, v. 56. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

†For previous articles on the typhus group of fevers in this series, see the October issues of the *Tropical Diseases Bulletin* each year since 1939.

reinfection rather than relapse; she observed that primary and recurrent cases occurred in similar circumstances, and that the patients often gave a history of long railway journeys, or of occupations connected with dirty linen or involving frequently changing contact with people, or of louse infestation during the incubation period. SHATROV (p. 932) does not believe that persistence of infection, or relapses, occur in typhus, but thinks that continuity of the disease is maintained by unrecognized infections treated under other diagnoses. Similarly, in Russia where the proportion of second attacks of typhus has risen in recent years, GUS'KOVA (p. 1016) does not believe that an attack confers lasting immunity; second attacks arise in subjects who have lost specific immunity, after contact with inapparent or mild cases. She also links susceptibility to typhus with low physiological reactivity in elderly persons.

Results of agglutination tests with rickettsial antigens in Tunisia indicate that *Rattus norvegicus* may be a reservoir of *R. prowazeki* and *R. burneti*, as well as of *R. mooseri* (JUMINER, p. 1226).

In an area of Rumania where typhus is endemic, COMBIESCO *et al.* (p. 287) show that the complement-fixation test is much more sensitive than the Weil-Felix test.

In using indirect fluorescent antibody staining for differentiating *R. prowazeki* and *R. mooseri* antibodies, GOLDWASSER and SHEPARD (p. 932) found that cross-reacting antibodies could be absorbed by diluting the sera with heterologous antigen, leaving the specific antibodies to react with homologous antigen.

WEISS *et al.* (p. 707) studied strains of *R. prowazeki* resistant to PABA and to dimethylquinoxaline dioxide; they resembled the parent strain in mouse toxicity, haemolysin production and antigenicity, but there was reduced virulence for chick embryos and cotton-rats. The studies may help the analysis of genetic events in rickettsiae.

ZDRODOVSKII (p. 602), after laboratory investigation, expresses the view that the Spanish strain E of R. *prowazeki* is suitable for use as a live vaccine for man. PSHENICHNOV *et al.* (p. 522) discuss a strain of *R. prowazeki* which had been attenuated by maintaining it in lice for 12½ years at 31–32°C.; it was then non-virulent for guineapigs, but provoked the formation of agglutinins in them and they resisted challenge with a virulent strain. It may therefore prove useful as a vaccine. KOCH and BENKÖ (p. 602) use carbon tetrachloride in the preparation of the Cox type of typhus vaccine from infected yolk sacs, and find it satisfactory.

Severe anaphylaxis is reported by WRIGHT (p. 813) in a patient inoculated with typhus vaccine (egg type); the patient had a long history of allergy to eggs, but had received many previous injections of egg vaccines without ill-effects. Two similar cases have been fatal, and these vaccines should not be given to persons suspected of allergy to eggs. AKAISHI (p. 1120) reports a child who died 10 minutes after typhus vaccination; she also was allergic to eggs.

In a cold mountainous part of Mexico, typhus occurred in winter until an intensive programme of dusting with DDT, and education, was carried out in 1955–56; since then no typhus has been reported, though ROBLES GARNICA (p. 428) reports that lice are still found on 25% of the people against a former incidence of 50–100%. COLE and CLARK (p. 26) write of compounds which act synergically with rotenone, for use against DDT-resistant lice on human subjects.

It has been suggested that when *R. mooseri* is maintained for many passages

in lice it may rapidly change to *R. prowazeki*, but experiments conducted by Balaeva (p. 27) do not support this view.

Greisman and Wisseman (p. 289) studied the effect of intravenous injection of the toxin of *R. mooseri* on the cardiovascular system of white rats. Details should be sought in the original.

Mohr (p. 290) analysed the relationship between the geographical and seasonal prevalence of fleas on rats in south-eastern United States, and the incidence of human cases of murine typhus. There was a relationship to high external temperature—which favoured infestation and human disease—and in the colder areas this was in part related to the artificial heating of buildings in the cold weather.

Proteus OXK Type. Vector: Mite

Levy (p. 1227) reports 2 cases of scrub typhus with genital eschar and regional adenitis in soldiers in Malaya; they could have been mistaken for venereal disease and he stresses the importance of including scrub typhus in differential diagnosis in the endemic areas.

Sasa (p. 143) discusses the chaetotaxy of the legs of larval trombiculid mites of Japan, including *Trombicula akamushi*. Morphological and biological differences between 2 types of *Trombicula deliensis* are described by Yü and Wu (p. 815).

Harrison (p. 933) explains his technique for studying the range of movement of various Malayan rats which might be associated with the vectors of scrub typhus. By observing the voles (*Microtus montebelloi*) marked and released on a patch of land in a scrub typhus area of Japan, Tanaka *et al.* (p. 815) showed that infestation with trombiculid mites is patchy over the land.

Hopps *et al.* (p. 814) show that although *R. tsutsugamushi* will grow in tissue culture of mouse fibroblast and lymphoblast, they will not do so if the culture cells are inadequately nourished. Chloramphenicol has a rickettsiocidal effect in such cultures, and certain amino acids suppress rickettsial growth at concentrations not toxic for the culture cells. Cohn *et al.* (p. 708) describe a system for observing quantitatively the penetration of *R. tsutsugamushi* into tissue culture cells, and discuss the factors which influence this.

Kawamura *et al.* (p. 602) have treated the ether-extracted *R. orientalis* and *R. tamiyai* antigens of the Cox-Craigie type with ethanol; they were not initially anti-complementary, but tended to become so on storage, though this effect could be removed by treatment with ether.

Indeterminate Type. Vector: Tick

Berni (p. 603) discusses boutonneuse fever, which occurs endemically in the Commune of Rome in summer, and is transmitted by *Rhipicephalus sanguineus*.

On an island of southern Primor'e Somov *et al.* (p. 523) observed a febrile illness resembling tick typhus, with an erythematous rash and a necrotic lesion at the site of the tick bite. Strains of a rickettsia were isolated from *Haemaphysalis concinna* and the sera of animals infected with it gave reactions to *R. sibiricus*, the agent of Northern Asian tick typhus. Shapiro (p. 1017) also isolated the organism from *H. concinna* on the same island, and from pools of mites and from *Microtus fortis*. Kireeva (p. 428) shows that agglutination of *Proteus OX2* at high titre is constantly found in North Asiatic tick typhus.

From Kenya TIMMS *et al.* (p. 816) describe a case, probably of tick typhus, in which the infection was almost certainly transmitted by *R. simus*. HEISCH and HARVEY (p. 1018) submitted to the complement-fixation test sera from guineapigs inoculated with strains of rickettsiae isolated from ticks in Kenya, and sera from certain wild rodents. The results show that the rickettsiae of tick typhus in East Africa and South Africa are closely related; the reservoir in East Africa may be a complex of rodents.

Immunological and serological studies indicated that the rickettsiae of Kenya and Indian tick typhus are identical with the Black Sea strain of *R. conori*, and the rickettsia of Marseilles fever (ZDRODOVSKII and GOLINEVICH, p. 708).

MISSIRLIU *et al.* (p. 1120) report cases of Rocky Mountain spotted fever in Tennessee children; in many of them rising titres to *Proteus OXK* were observed.

WEYER (p. 291) observed that *R. rickettsi* from Brazil and a rickettsia of Siberian tick-bite fever were able to multiply in body lice and to persist in them for long periods without loss of virulence. They also developed in several other arthropods, but not in bed-bugs.

Q fever

R. burneti has been isolated from the pooled milk of cattle in many parts of Britain, but infection rates are low as judged by serological tests; MARMION and STOKER (p. 144) recall that antibodies have also been found in sheep and hens, and *R. burneti* in sheep placentas and in ticks in Kent. The disease has been observed in man in middle and southern England, and is related to cattle and sheep, though spread from sheep to man may not always take place by the most direct route.

Q fever is also reported from the following places:—

Place	*Authors*
Sardinia	ANGELILLO *et al.*, p. 429
Dalmatia	VESENJAK *et al.*, p. 145
Yugoslavia	GAON and GALL, p. 291
Poland	OLÉS, p. 27; WOJCIECHOWSKI, p. 1018
U.S.S.R.	
Voronezh	DOLGOV, p. 817
Armenian S.S.R.	KOTSINIAN, p. 523
Kirghiz S.S.R.	LASHKEVICH, p. 818
Tartar area	VAINSHTEIN *et al.*, p. 817
Tripolitania	MODICA and COSTA, p. 816
Dakar	BAYLET *et al.*, p. 146
Quebec	PAVILANIS *et al.*, p. 524
Arizona	DI SALVO and WERTMAN, p. 146
Iowa	TJALMA and SMITH, p. 430
Idaho	STOENNER *et al.*, p. 1121
Queensland	DERRICK *et al.*, p. 1019

In these places it is associated with domestic animals—cattle, sheep, goats—and occurs in persons such as farm workers and meat handlers, who deal with such animals.

REHN and RADVAN (p. 604) have isolated *R. burneti* from a shrew mouse in Bohemia. ZARNEA *et al.* (p. 1227) found it in the hedgehog *Erinaceus europaeus* in Rumania; the infection was probably present in the animals on which it feeds—insects, small rodents etc. PAVILANIS *et al.* (p. 524) isolated it from *Melophagus ovinus*, a parasite of sheep, which only accidentally feeds on man or other animals.

SILICH (p. 147) observes that infection with *R. burneti* can be acquired through contact with infected meat and blood, and that the organism retains its vitality in meat during refrigeration for at least 30 days, and in salted meat for much longer.

REHN (p. 29) successfully infected foxes and forest mice with *R. burneti;* viraemia was observed in the foxes for 30 days and the mice for 12. He (p. 431) shows that ticks (*Ixodes ricinus* and *Dermacentor pictus*) can be infected by feeding on infected animals, that their faeces contain the rickettsiae during engorgement, and that transovarial transmission can occur. Animals may be infected by ingestion of infected ticks or inhalation of their faeces.

Hyalomma plumbeum plumbeum is a successful vector of *R. burneti*; TARASEVICH (p. 28) obtained light infection by feeding them on infected guinea-pigs, but much heavier infection by injection into the haemocoele.

ROBERTS and DOWNS (p. 709) show that *R. burneti* can grow in tissue cultures of strains of mouse fibroblasts and chick fibroblasts, but not in cell-free medium or in cell debris. Growth was inhibited by streptomycin at a concentration of 0·5 mgm. per ml.

BREZINA (p. 604) observed that the egg-adapted strain of *R. burneti* showed increased virulence for guineapigs after intraperitoneal passage in mice. The antigenicity of this strain was also increased, and this may be significant in connexion with the selection of strains for vaccines.

Ultrafiltration experiments indicate that filtrates of suspensions of *R. burneti* may remain infective after being passed through membranes of mean porosity down to 65 mμ, and that typical rickettsiae may develop from such filtrates on passage in yolk sacs (KORDOVA, p. 710).

BREZINA (p. 292) discusses phase variation in *R. burneti*; details should be sought in the original abstract; PARETSKY *et al.* (p. 27) discuss the enzyme systems.

ZUBKOVA (p. 292) shows that *R. burneti* survives for long periods in milk at room temperature, and that the existing methods of pasteurization are not satisfactory; the organism survives heating at 90° [C.] for 1 hour in unskimmed milk. *R. burneti* can survive for up to 15 days on glass and other surfaces; KULAGIN *et al.* (p. 711) report on the action of various disinfectants on contaminated surfaces. Boiling for 30 minutes and soaking for 1 hour in 5% phenol, 3% chloramine or 3% "KhB" [not defined] killed them. A high concentration of formalin is needed. They (p. 430) discuss the dosage of chlorine in water required to kill *R. burneti*. Details should be sought in the original.

R. burneti is relatively resistant to various chemicals, for instance 1% of formaldehyde, 5% acetic acid, 5% sodium hydroxide and 3% hydrogen peroxide; solutions of these which are twice as strong are rapidly lethal (SOKOLOVA and FEDOROVA, p. 711).

Increased resistance to *R. burneti* has been observed in guineapigs infected with *Brucella suis*, but MIKA *et al.* (p. 293) do not think that this interference phenomenon can be explained on the basis of demonstrable immunological

factors. PIRSCH *et al.* (p. 712) also show that injection of *Brucella suis* endotoxin into guineapigs interferes with subsequent infection with *R. burneti*; this effect can be nullified by treatment with cortisone.

BABUDIERI (p. 524) has compared the microscopic slide agglutination test for *R. burneti* with the complement-fixation test, the macroscopic tube test and the capillary tube test; for sheep the microscopic slide agglutination test was by far the most sensitive. It can be performed satisfactorily with an extract of a drop of dried blood on filter paper; and for man, inactivation at 56°C. before testing is advocated, to eliminate a heat-labile inhibitor believed to be identical with complement. KORDY (p. 524) used the micro-complement-fixation test for Q fever in Egypt, and found positive results in adult persons, and in sheep and camels. In investigations in Yugoslavia, GERBEC *et al.* (p. 604) maintain that positive complement-fixation tests, with undiluted serum, were specific, and did indicate previous contact with *R. burneti*.

ANGELILLO *et al.* (p. 1227) found that the conglutination reaction corresponded closely with the complement-fixation reaction for the diagnosis of Q fever in bovine sera.

A fatal case of infective endocarditis in which *R burneti* was isolated from the aortic valve is reported by EVANS *et al.* (p. 818).

FEDOROVA *et al.* (p. 819) used a formalin vaccine of *R. burneti* which had been stored for 20 months at 4°C., and observed that it caused relatively mild reactions though retaining immunological effectiveness. SHIFRIN *et al.* (p. 819) have used a formalin *R. burneti* vaccine for lambs, with success in stimulating the formation of antibodies.

Reactions to *R. burneti* vaccine which had been stored for 15 months were fewer than to vaccine stored for 3–4 months; for mass vaccination KULAGIN *et al.* (p. 1121) recommend 2 doses at an interval of 2 weeks. It is thought that the most effective means of controlling Q fever in Central Asia is by vaccination, and BELIAKOV and IL'CHENKO (p. 1122) have used a vaccine which includes enteric organisms and tetanus toxoid in addition to *R. burneti*.

Rickettsialpox

KISELEV and BEKKER (p. 603) discuss the allergic component of fractions isolated from *Dermacentroxenus murinus*, the organism of rickettsialpox.

Charles Wilcocks

MALARIA

In this section abstracts are arranged as far as possible in the following order:—Human malaria—*epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control;* Animal malaria—*monkeys, other animals, birds.*

COVELL, G. **Relationship between Malarial Parasitaemia and Symptoms of the Disease. A Review of the Literature.** *Bull. World Health Organization.* 1960, v. 22, No. 6, 605–19. [Numerous refs.]

The literature on the relationship between parasitaemia and the clinical effects of malaria; immunity; the pattern of gametocyte prevalence at various

stages of an infection; the degree of gametocytaemia necessary for man to be infectious to the mosquito, and the length of survival of the parasite in the human host, are reviewed in this paper, to which an abstract can do scant justice.

The importance of asymptomatic parasitaemia as a major factor in the transmission of malaria has been emphasized since the beginning of the century. STEPHENS and CHRISTOPHERS in Africa, Robert KOCH in Africa and Java, BERESTNEW in Russia, and indeed surveys wherever the disease is endemic indicated the wide prevalence of asymptomatic parasitaemia particularly in infants and small children. Repeated and prolonged blood examination often reveals minimal parasitaemia, which though apparently asymptomatic has been found to be associated with low grade pyrexia. That the proportion of fever cases is an indication of the degree of malarial infection in a community has been demonstrated on several occasions. Prolonged studies of parasitaemia have been made. In Liberia, 19 out of 20 adults were found to have positive bloods at some time during a year's observations, the number of days positive varying from 1 to 294, average 76 [this *Bulletin*, 1958, v. 55, 974]. 32 clinical attacks caused an average of 6·5 days' morbidity per person per year. [The figure of a week's mild illness a year for adults in holoendemic areas is widely quoted, though some workers, including COLBOURNE who is not quoted in this paper, have suggested 5 days in 7-year-old children and 1 or 2 days in adults.] In Nigeria, 35 out of 70 subjects studied showed mild clinical symptoms within 1–2 years, though only 5 had negative bloods throughout. Deliberate superinfection of 22 subjects with a possibly heterologous *Plasmodium falciparum* strain produced symptoms in only 4, but a temporary wave of parasitaemia in 16. Afebrile parasitaemia of 10,000 per cu.mm. has been reported.

Gametocyte production was thought by Koch in 1898 to be a response to the process of immunization, a theory not contradicted until 1919 by Schüffner, who proved that the reverse is the case. In holoendemic areas gametocytaemia is by far the commonest in small children, but in areas affected by acute epidemic conditions people of all ages are equally parasitized and all present high gametocyte counts. Several observers have commented on the rarity of gametocytaemia before and at the beginning of the malaria epidemic season, but mathematical analysis shows that a 5·0% rate could produce one of 50% by the ninth week of enhanced transmission. Even in holoendemic areas there are wide seasonal variations in gametocyte rates. A positive correlation has been noted between the numerical prevalence of asexual parasites and the number of gametocytes appearing some 10 days later. The longevity of individual crescents has been variously estimated at 20 to 60 days, but gametocytaemia can persist in the absence of clinical attacks, and its presence in the later stages of a malarial infection appears to be unpredictable. In *P. falciparum* and *P. vivax* infections, levels of gametocytaemia too low for detection by routine blood examination can infect mosquitoes, and these low grade infections are thought to be epidemiologically important. In *P. malariae* a higher level is necessary. The bulk of available evidence suggests that in the great majority of cases the limit of infectiousness of *P. falciparum* does not exceed 1 year and of *P. vivax*, 2 years. However, it has become obvious that the only way in which a valid assessment of the infectivity of a community can be obtained is by feeding

mosquitoes on a representative sample of the population—a procedure presenting considerable practical difficulties. *B. B. Waddy*

GARLICK, J. P. **Sickling and Malaria in South-West Nigeria.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Mar., v. 54, No. 2, 146–54, 2 figs. [18 refs.]

Three groups of children were tested at Adeoyo Hospital, Ibadan, (a) 244 aged ½ to 6 years, attending for "fever", (b) 189 from the same clinic selected as controls, (c) 172 aged 5 to 9 years attending a school nearby.

It was notable that the sickling rate in those complaining of fever was 15·2%, while in the other groups it was 28·6 and 31·4% respectively.

Crude parasite rates in groups (a) and (b) were lower, but not significantly so, in the sicklers, but were equal for sicklers and non-sicklers in group (c). However, in all 3 groups the rates for *Plasmodium malariae* were lower in sicklers, and this difference was noted at all ages. It is the first time that this effect has been recorded. With *P. falciparum*, sicklers in groups (a) and (b) *under the age of 3* showed significantly lower rates than non-sicklers, an advantage that disappeared after the age of 3.

Parasite density measurements for *P. falciparum* again showed lower figures for sicklers, but these only attained statistical significance in group (b), or when the whole series was divided into those with counts below 100/cmm. and those with counts above this level.

An interesting enquiry was made into the possibilities (i) that there is an increased mortality of non-sickling children, and (ii) that sickling mothers have enhanced net fertility. In the hospital clinic, the sickling status of mother and child was determined for 605 pairs, ascertained through the child. Then, based on a generally accepted sickling rate of 26% for adults in Ibadan, and assuming that none of the children were homozygotes, the expected sickling rate for the mothers was calculated on each of the above hypotheses. These calculated rates were of course different, and it was found that the observed rate fell about halfway between them. On these results the author comments "The χ^2 test shows it to be improbable that differential fertility is solely responsible for the heterosis. The fit between the observed values and those predicted by the differential viability hypothesis is satisfactory, so that there is no necessity to invoke differential fertility to explain the results. But the observations would, of course, fit best a heterosis involving both mechanisms".

[See also this *Bulletin*, 1959, v. 56, 592.] *Alan B. Raper*

GARNHAM, P. C. C. La ricerca del ciclo eso-eritrocitico nella malaria dei mammiferi. [**Research on the Exo-Erythrocytic Cycle in Mammal Malaria**] *Rendiconti Istituto Superiore di Sanità.* Rome. 1959, v. 22, Pts. 11/12, 1189–99, 21 figs. on 4 pls. & 2 text figs.

Garnham describes his team's standard technique for the demonstration of the exo-erythrocytic cycle of malaria parasites. This technique is a team operation in which the time factor is all-important, calling for very careful planning and execution. The experiments are more difficult with some species than with

others because of the strictly specific nature of the parasite-host relationships. There have been various modifications tried for the purpose of overcoming the difficulties and disadvantages met with: the mosquitoes have been fed with para-aminobenzoic acid, suspensions of mature oöcysts have been inoculated intravenously, *Anopheles aztecus* from Mexico has been tried as the vector but found difficult to rear in London, and the chimpanzee has been employed as a host at a London price of £200!

The main characteristics of 7 species of *Plasmodium* in their early stages after invasion of man and monkey are briefly discussed and the author stresses the specific appearance of the exo-erythrocytic forms in the liver. He has received microscopic sections from fellow-workers, without any other information, and he has been able to determine the age of development as well as identify the species of *Plasmodium*.

There is a brief account of FAIRLEY'S experiments, carried out some 15 years ago with human volunteers, which demonstrated the "latent" phase of *P. vivax* (8 days) and *P. falciparum* (5 days). Fairley has since pointed out the risk of giving suspensions of sporozoites intravenously to human volunteers; strains of resistant staphylococci may have found their way into such suspensions in the course of preparation. *J. Cauchi*

SENEVET, G. & CLASTRIER, J. Présence d'*Anopheles* (*Anopheles*) *claviger* Meigen var. *petragnani* del Vecchio dans le Sud-Est de la France. [*A. claviger* **var.** *petragnani* **in South-Eastern France**] *Arch. Inst. Pasteur d'Algérie*. 1960, Mar., v. 38, No. 1, 112–16, 2 figs. [22 refs.]

Anopheles claviger is recorded in the literature from many parts of France. Several variants have been recognized to exist in Spain (var. *pollutus*), Italy (var. *missiroli* and var. *petragnani*), Algeria (*sahelensis*—a race of *petragnani*) and France. A description is given of setal characters of larvae and pupae for differentiating var. *missiroli* and var. *petragnani*, both of which can be expected to occur in France. The present record for the latter is from near Nice. Biological differences between variants are such as to make one, but not another, amenable to laboratory culture. *D. S. Bertram*

RANQUE, J., RIOUX, J. A., QUILICI, M., RANQUE, P. & NICOLI, R. M. Anophélisme et indice splénique dans le site de Porto-Vecchio (Corse) durant l'été 1959. Étude comparative avec les données antérieurement connues. [**Anophelism and Splenic Index in Porto-Vecchio, Corsica during the Summer of 1959. Comparative Study with Earlier Data**] *Bull. Soc. Path. Exot.* 1959, Nov.–Dec., v. 52, No. 6, 808–19, 2 maps. [Numerous refs.]

This paper contains a short review of the antimalarial campaigns at Porto-Vecchio, Corsica, since the first campaign in 1911 to eradication between 1947 and 1953. In 1959 anopheline larvae were found in fresh and saline breeding places, which are illustrated by 2 maps. In 300 children, aged 5–18 years, 13 showed enlarged spleens and 5 of these children had never left Porto-Vecchio and its surroundings. *B. R. Laurence*

SENEVET, G., BERNET, J., CLASTRIER, J. & ABONNENC, E. Présence d'*Anopheles* (*Myzomyia*) *d'thali* Patton en deux régions de l'Afrique voisines de l'Atlantique. Sa répartition géographique sur le Continent africain. [*A. dthali* **in Two Atlantic Regions of Africa: Geographical Distribution in Africa**] *Arch. Inst. Pasteur d'Algérie*. 1960, Mar., v. 38, No. 1, 106–11, 1 map. [27 refs.]

A useful map, the text and a footnote provide new records for *Anopheles dthali*, showing that it occurs quite widely in suitable places in north Africa in the Sahara belt, notably westwards to the Atlantic coast of Mauritania.

D. S. Bertram

MAFFI, M. Focolaio larvale de *A. gambiae* e di *A. squamosus* in raccolta d'acqua salata, a Busc Busc (fascia costiera del basso Oltre Giuba). Primo reperto in Somalia. [**Larval Breeding Places** *Anopheles gambiae* **and** *A. squamosus* **in Collections of Salt Water in Busc Busc, Somalia**] *Riv. di Malariologia*. 1960, June, v. 39, Nos. 1/3, 131–3.

The English summary appended to the paper is as follows:—

"The author reports the first findings in Somalia of salt water breeding of *A. gambiae* and of *A. squamosus*.

"The breeding place was a well—abandoned because of inleaking of salt water—10 feet deep, at the limit of the mangrove belt fringing the Bubasci estuary, near Busc Busc, a hamlet of the lower Jubaland.

"Water was scarcely a foot deep; salinity was 14·6 g NaCl per litre.

"This is the furthest north that salt water breeding of *A. gambiae* has been reported on the African East Coast; and probably does not represent the northern limit.

"*A. squamosus* has not been reported from such waters before."

RIOUX, J. A. & PECH, J. *Coelomomyces grassei* n.sp. parasite d'*Anopheles gambiae* Giles (note préliminaire). [Miscellanea.] [*Coelomomyces grassei* **n.sp. a Parasite of** *Anopheles gambiae*] *Acta Tropica*. Basle. 1960, v. 17, No. 2, 179–82, 3 figs. [12 refs.]

See also p. 1120, GOMA, **The Swamp-Breeding Mosquitos of Uganda: Records of Larvae and their Habitats.**

MAURITIUS, COLONY OF. **Annual Report of the Medical and Health Department 1957. Appendix V. Report of the Entomologist for the Year 1957. Insect-Borne Diseases Division** (pp. 66–88). 100 pp. 1959, Apr. Port Louis: Govt. Printer. [R.1.25.]

——. **Annual Report of the Medical and Health Department 1958. Appendix IV. Insect-Borne Diseases Division. Report of the Entomologist for the Year 1958** (pp. 49–55). 70 pp. 1959, July. Port Louis: Govt. Printer. [R. 1.]

These two successive Annual Reports were received and are abstracted together. There are puzzling and conflicting results in data for hosts of *Anopheles gambiae* and *Culex pipiens fatigans* which require further investigation. This is apparently in progress. Insecticides are barely mentioned in the 1958 report.

Data are tabulated (1957) for all-night catches outdoors on human bait of *Anopheles gambiae, A. coustani, Culex p. fatigans, C. tritaeniorhynchus, Aëdimorphus fowleri* and *Aëdes albopictus.* This last species, mainly diurnal, bit during the night in small numbers. The other species are nocturnal and some particularly late evening, or crepuscular feeders. Catches are shown for hourly intervals. They are totalled for 14 to 46 nights; in 14 nights 2,954 *A. gambiae* were taken, over 1,200 *A. coustani* in 46 nights, and fewer of the other species. Host preferences between man, domestic animals and fowl were studied by the precipitin test—conducted by the Division with proprietary antisera—in mosquitoes collected from cowsheds, houses, crevices in walls around cattle pens or taken in the night catches referred to above. With some allowance conceded in the last particular for engorgement on the human bait, the conclusion is reached that *A. gambiae* taken outdoors in 1957 had most often fed on man. Cattle were usual hosts too, less often goat, hen or dog; both human- and cattle-fed mosquitoes rested in cattle sheds and in houses. But there was some dissection for ovarial development which suggested that females prefer the dark and more humid cattle sheds and outdoor resting places for complete gonotrophic development, and tend not to wait in the lighter, airier houses longer than allows the early stages of egg development. This interesting observation on outdoor anthrophily recorded in the 1957 report is also postulated as being possibly explicable by the inclusion in outdoor catches of human-fed females transferring from houses to elsewhere [? or having left or leaving houses after contact with DDT]. The 1958 report gives further results on precipitin tests of 188 *A. gambiae* taken out of doors from bushes and wall crevices (in 1957, those caught outside and tested numbered 298), but the result was contradictory, the majority having fed on bovines, a few only on man, occasionally on dog. This remains unexplained, but the work will be continued. [An Advisory Team of WHO visited the island during early 1958 and its assistance in planning the work reported for 1958 may be deemed to give these data greater critical worth.] In 1957, precipitin tests indicated *C. p. fatigans* to have a preference for man, although feeding on fowl. Again, however, the 1958 data gave the opposite result.

The more recent of the reports is much the shorter. It gives interesting emphasis to outdoor resting places of *A. gambiae,* which include thick walls with deep crevices (15–18 inches deep) where the mosquitoes retreat by day. Although the 1957 report submits data on DDT susceptibility of *A. gambiae* and concludes that vigour tolerance is apparent, insecticides are not mentioned in the 1958 account of entomological work except to note resting of this species in untreated cowsheds, or cowsheds with little residual effect remaining. Regarding malaria, no sporozoites were found (in 1958) in 430 *A. gambiae,* 1,094 *A. coustani* and 5 *A. maculipalpis* dissected between June and December. This work continues.

The much larger 1957 report notes, besides the subjects referred to already, that no relationship existed between maxillary indices for *A. gambiae* fed on man or cattle; laboratory survival of bred *A. gambiae* (about 17 days) and *A.*

coustani (about 10 days); insusceptibility of *C. p. fatigans* to DDT; laboratory culture (method described) of rearing *Musca*; successful kill of flies in hospital premises with diazinon-treated cords for 6–7 weeks; and laboratory trials of Malatox and Muscatox against the laboratory strain of *Musca*. In this, Muscatox was effective for up to 10 weeks, but Malatox only for about a week.

D. S. Bertram

MALAYA, FEDERATION OF: Institute for Medical Research, Division of Entomology [REID, J. A. *et al.*]. **Pictorial Key to the Principal Anopheles of Malaya. [i] Larvae. [ii] Adult Females.** 2 folding sheets. [?1960.] Kuala Lumpur.

DORANTES, S., SOTO, R. & BIAGI F., F. Un caso de anemia africana con esquizontes de *Plasmodium falciparum* en sangre periférica. [**A Case of Sickle-Cell Anaemia with *Plasmodium falciparum* Schizonts in Peripheral Blood**] Reprinted from *Bol. Méd. Hosp. Infantil.* Mexico. 1960, v. 17, No. 2, 229–37, 3 figs. [25 refs.]

The English summary appended to the paper is as follows:—

"The finding of schizonts of *P. falciparum* in the peripheral blood of a child with sickle cell anemia is reported. The patient carried its malaria quite well, and had a low parasitemia. The possible cause for the finding is discussed."

JANSSENS, P. G. & RAVESCHOT, J. Nopens een geval van malaria- of carentiële encefalopathie. [**A Case of Encephalopathy due to Malaria or Malnutrition**] *Ann. Soc. Belge de Méd. Trop.* 1960, Feb. 29, v. 40, No. 1, 231–6.

The English summary appended to the paper is as follows:—

"A Wernicke type encephalopathy accompanied by anorexia and vomiting is described, occurring in a patient suffering from severe prolonged malaria due to *P. falciparum*. Complete proof of a direct malarial action could not be provided though the rapid improvement of the very grave state of the patient even before restoration to a correct dietary regime, suggests that it cannot be regarded as being due purely to deficiency. It appears therefore that an encephalopathy of the type described must now be included in the protean symptomatology of malaria."

GILLES, H. M. & HENDRICKSE, R. G. **Possible Aetiological Role of *Plasmodium malariae* in "Nephrotic Syndrome" in Nigerian Children.** *Lancet.* 1960, Apr. 9, 806–7, 1 fig.

The nephrotic syndrome has been noted so frequently in children attending the pediatric department of University College Hospital, Ibadan, Nigeria, that a special "nephrotic clinic" has been set up. In 9 months 48 fresh cases of this

condition were recorded. By contrast, among all children attending three large hospitals in Durban, South Africa, only 12 " nephrotic " children were seen in 18 months.

This preliminary communication reports the result of investigations carried out on these 48 children.

The clinical picture, typified by an excellent photograph comprises gross oedema, massive albuminuria, severe hypoproteinaemia [better expressed as hypoalbuminaemia, as none of the globulin fractions were significantly diminished], no nitrogen retention and a normal blood pressure. The mean serum albumin concentration was 0·62 (range 2·04–0·06) gm. per 100 ml., while in " normal Nigerian children " the corresponding value was 3·20 gm. per 100 ml. The serum cholesterol concentrations showed wide variation, with a mean of 265 mgm. per 100 ml. in the " nephrotic " group, compared with 101 mgm. per 100 ml. in the control group.

Percutaneous renal biopsy on 18 patients produced specimens on which Professor G. M. EDINGTON has made a preliminary report as follows: " In general it can be said that the renal biopsies showed uniform histopathological changes. There were patchy lesions of varying severity in the glomeruli with associated tubular degenerative changes. Round cell infiltration of the interstitial tissue of varying severity was an inconstant finding. The overall picture is similar to that described in an Ellis type II nephritis ".

Recalling the demonstration by GIGLIOLI [this *Bulletin*, 1930, v. 27, 508] in British Guiana of an association between *Plasmodium malariae* infection and the " nephrotic " syndrome, the authors sought such an association in this series. The incidence of parasitization by *P. malariae*, by *P. falciparum* or by *P. malariae* and *P. falciparum* together, was determined in the 48 " nephrotic " patients, in a group of 800 non-nephrotic sick children and in 200 " healthy " children from a neighbouring village. The incidences are set out in a table, from which the most significant are as follows:—

	Overall *P. malariae* infection rate	*P. falciparum* only
nephrotic children	89·6%	2·1%
non-nephrotic sick children	24·0%	52·0%
" healthy " children	23·0%	44·0%

[The inference that a causal association exists between infection with *P. malariae* and the " nephrotic syndrome " seems inescapable to the abstracter.]

To date, antimalarial treatment has not significantly influenced the course of the disease in a treated group as compared with an untreated group.

J. H. Walters

CARTER, F. S. *Plasmodium malariae* **in " Nephrotic Syndrome ".** [Correspondence.] *Lancet*. 1960, May 21, 1128–9.

The author, who writes from Aden, refers to the report of GILLES and HENDRICKSE on the relationship between the nephrotic syndrome and *Plasmodium malariae* infection in Nigerian children [see above].

In the period November 1955 to September 1959, he had been in Freetown, Sierra Leone, and during that time saw only 3 cases of nephrotic syndrome in children under 10 years old. From March to August 1959, of 422 children admitted there were 54 proved cases of malaria, all due to *P. falciparum*, which is virtually the only species seen in the Freetown area. The virtual absence of *P. malariae* and of the nephrotic syndrome in Freetown seems to support the aetiological role of this species of malaria parasite in the syndrome, especially as Nigeria and Sierra Leone have so many paediatric problems in common.

H. J. O'D. Burke-Gaffney

LYSENKO, A. Y. **Use of Quinocide in Treatment and Prophylaxis of Vivax Malaria.** *Bull. World Health Organization.* 1960, v. 22, No. 6, 641–62, 5 figs. [30 refs.]

Quinocide (=Chinocid), a member of the 8-aminoquinoline series of compounds, was synthesized in 1952 at the Martsinovski Institute of Medical Parasitology and Tropical Medicine of the U.S.S.R. Ministry of Health, Moscow. It differs from primaquine in the position of the methyl group in the side-chain but has similar antimalarial properties. Clinical and field trials were completed during the next 4 years and by 1957–58 the drug had been taken into general use throughout the malarious tracts of the U.S.S.R.

An account is given of experiments carried out to test the physicochemical properties of the drug, its pharmacology, the frequency and nature of side effects when given either alone or in combination with other antimalarial drugs and its parasiticidal activity.

The toxicity of Quinocide for animals is considerably less than that of plasmocide (=pamaquine) and in therapeutic doses in human subjects obnoxious side effects are infrequent and rarely necessitate cessation of treatment. The simultaneous administration of Quinocide with other antimalarials is not however recommended. In animal experiments the most severe toxic symptoms were noted when the drug was given in combination with Chlorodine (=pyrimethamine).

By reason of its success in the prevention of relapse and its sporontocidal and prophylactic properties, Quinocide is considered particularly suitable for the clearance of malarial foci in the later stages of an eradication campaign and for the elimination of foci which may recur in previously cleared territory. Radical anti-relapse treatment and prophylaxis with Quinocide was practised on a large scale in Tadzhikistan in 1955–57, but since imagocides were also extensively used in this campaign it is not easy to assess with accuracy the specific part played by the drug. That its influence was very considerable is however indicated by the fact that morbidity during the first half of the year was greatly reduced in comparison with other areas where Quinocide was not widely used.

The results of extensive trials to test the antimalarial properties of Quinocide have been reported in a number of previous papers by the author and his associates [this *Bulletin*, 1956, v. 53, 16; 1957, v. 54, 924]. The results of these studies are shown in tables and reported very fully. *G. Covell*

BREWER, G. J., TARLOV, A. R. & ALVING, A. S. **Methaemoglobin Reduction Test. A New, Simple,** *in vitro* **Test for Identifying Primaquine-Sensitivity.** *Bull. World Health Organization.* 1960, v. 22, No. 6, 633–40, 1 fig. [14 refs.]

Primaquine sensitivity results from a genetic defect which is characterized by a deficiency of glucose-6-phosphate dehydrogenase. In those who suffer from this defect intravascular haemolysis may result from ingestion of certain drugs or foodstuffs. Various tests for this type of sensitivity have been described. The GSH stability test is widely used [BEUTLER *et al.*, this *Bulletin*, 1955, v. 52, 510, 610; *J. Clin. Invest.*, 1957, v. 36, 617], also the dye test of MOTULSKY *et al.* (*Clin. Res.*, 1959, v. 7, 89) in which the haemolysed cells fail to affect the colour of brilliant cresyl blue. In both tests the above dehydrogenase is involved.

In the present communication two modifications of a new test known as the methaemoglobin reduction test for primaquine sensitivity are described. One of these is used as a " field screening test " in which methaemoglobin is reduced to haemoglobin. It is simple to carry out and of practical value when surveys are being made. The other clinical test requires optical apparatus such as a photo-electrical colorimeter or spectrophotometer, and primaquine sensitivity is assessed by the failure of red cells to speed the reduction of methaemoglobin on incubation in presence of glucose, nitrite and methylene blue. The method of collecting and storing blood and the preparation of solutions required are described in detail. The rationale of these tests is also described but must be read in the original. The tests have been found of value in malaria eradication studies by drugs. *J. D. Fulton*

FUHRMANN, G. **A Field Test for the Estimation of Chloroquine in Urine.** *Bull. World Health Organization.* 1960, v. 22, No. 6, 663–8, 2 figs. [10 refs.]

When drugs are used for mass prophylaxis on malaria the problem of ensuring that they are regularly taken is a very real one. The author now describes the modification of an earlier test by which chloroquine can be estimated in 0·25 to 0·95 mgm. amounts per 100 ml. of urine [this *Bulletin*, 1951, v. 48, 95]. Earlier methods of estimation of value in the laboratory have also been described [*ibid.*, 1947, v. 44, 793; 1958, v. 55, 980].

The present test is suitable for use in the field and depends on the reaction of chloroquine base, extracted from urine by petroleum, with the Mayer-Tanret reagent which consists of a mixture of mercuric iodide and potassium iodide in the ratio 1 : 4. The turbidity produced is used to estimate the amount of base present by use of a calibration curve. The test is however not specific as proteins and other quinolines react and controls have to be used. A list of equipment necessary for carrying out 20–30 estimations per day under field conditions, including a colorimeter needing no electric current, is given and also the chemical reagents required. Urine, preferably a 24-hour specimen, must be freed of albumin by boiling and then filtered. Tables show the excretion of the drug in man after a single 300 mgm. dose, and other tables provide data to determine the amount of base present when the conditions specified are used. *J. D. Fulton*

YEKUTIEL, P. **Problems of Epidemiology in Malaria Eradication.** *Bull. World Health Organization.* 1960, v. 22, No. 6, 669–83, 1 fig. [16 refs.]

The various malaria eradication programmes now in progress in different parts of the world have brought to light certain problems peculiar to low-level transmission of the disease. Special measures are necessary to overcome the last small but often obstinate obstacles to eradication, and the conventional methods of malariometry formerly employed have been found inadequate for the year-by-year assessment of the general volume of malaria persisting in the population.

Data obtained through malariometric sample surveys are useful in the preparatory phase of a malaria programme and also in the first 2 years of the attack phase. But when parasite rates have dropped to a level of 1 to 3% it is necessary to adopt a system of malaria case detection, generally referred to as *surveillance*. Basically the process is one of continuous search for cases by the examination of blood films from all patients encountered with fever. This can be done either through a system of *active detection*, in which personnel of the malaria eradication programme visit all houses at regular intervals, or by one of *passive detection* whereby patients visit medical dispensaries or fever posts operated by voluntary collaborators in which blood films are taken, or by a combination of both systems. The total number of malaria cases detected during 1 calendar year expressed as a proportion of the total population constitutes an *incidence rate*, and this is considered to be the only reliable basis of assessment in malaria eradication programmes when the critical point of withdrawal of spraying operations is approached, and during the consolidation phase.

As regards criteria for cessation of spraying, these were laid down in the 7th Report of the WHO Expert Committee on Malaria [this *Bulletin*, 1959, v. 56, 921] as (a) interruption of transmission and (b) reduction of malaria cases to zero, or at least to a level so low that endemicity cannot readily be re-established. In practice these principles have been found unsatisfactory in that no quantitative measurements are given for guidance. The author holds that quantitative guidance in this matter is most necessary and believes that some conclusions can already be drawn from field experience acquired during the past 2 or 3 years. For example, in areas where consolidation has been successfully maintained after withdrawal of spraying, annual incidence rates per thousand of population have invariably been below the figure of 0·5. This level is obviously permissible only at the beginning of the consolidation phase and the result of surveillance should show a steady decrease of the figure towards total eradication within the prescribed time of 2 or 3 years.

Other problems discussed in this paper are those of asymptomatic parasitaemia, movements of population and mosquito behaviour. It is not always possible to reach a reliable assessment of the progress of a campaign by parasitological methods alone, and the author believes that the inclusion of comprehensive entomological data, showing not only the absence or greatly reduced number of anopheline vectors in sprayed houses, but also the effect of the spraying on the age distribution (survival rate) of the vector populations and on their indoor and outdoor man-biting rates, might render possible an earlier and even more reliable indication of interrupted transmission.

G. Covell

MACDONALD, G. L'eradicazione della malaria. [**The Eradication of Malaria**] *Rendiconti Istituto Superiore di Sanità*. Rome. 1959, v. 22, Pts. 11/12, 1200–211.

The author surveys the implications of programmes of malaria eradication in the light of what we have learned from research and other experience to date. Their planning must take account of the epidemiology of the disease in the territory and community involved. The toxicology of the insecticides to be used and the reaction of the mosquito species concerned, including the development of resistance and resistant strains, are very important factors. Combinations of several insecticides may prove successful in a particular case when each of these insecticides used by itself is ineffective. Our chemotherapeutic resources are now highly efficient, and an eradication plan must include a search for, and treatment of, all cases of infection if the "reservoir" is to be eliminated; and this is a link of the chain or cycle which must be removed. At a later stage, any reappearance of infection has to be spotted immediately and dealt with; the rate of spread in such cases becomes a vital element and must be investigated.

An eradication programme should provide for assessment of the problem, attack, consolidation and maintenance of control; every detail of administration must be carefully prepared and carried out if the programme is to succeed. The support of local authorities has to be obtained and their active cooperation is often essential. *J. Cauchi*

GARMS, R. Die Empfindlichkeit von *Anopheles atroparvus* and *A. stephensi* (Larven und Imagines) gegenüber DDT in Abhängigkeit von Alter, Ernährung und Populationsdichte. [**Susceptibility of** *Anopheles labranchiae atroparvus* **and** *A. stephensi* **to DDT in Relation to Age, Nutrition and Population Density**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1959, Dec., v. 10, No. 4, 426–41, 2 figs. [Numerous refs.]

Any critical work on the development of resistance or vigour tolerance in mosquitoes depends on reliable measurements of normal susceptibility of the species concerned. But mosquitoes are very labile in their physiology and this, in turn, affects their susceptibility levels. This is shown by previous work, especially with *Aëdes aegypti* and *Anopheles quadrimaculatus*. The present paper describes investigation of influence of certain factors on results of tests with larvae and adults of *Anopheles labranchiae atroparvus* and *A. stephensi*, from laboratory colonies.

The larval tests were done by the WHO method [this *Bulletin*, 1959, v. 56, 491]. In both species, the susceptibility declined as the larval development proceeded. For DDT the increase in tolerance was 10 times with *A. l. atroparvus* and 60 to 100 times with *A. stephensi*. In both species, the tolerance of dieldrin increased about 10 times from the 1st to the 4th stage. The very big increase in DDT tolerance of 4th stage *A. stephensi* suggests that this stage is likely to give erratic results and that the 3rd stage would give a more reliable basis for comparison.

Further tests were made of the effects of larval density during development on the susceptibility of 4th stage larvae. It was found that overcrowding

greatly reduced tolerance of DDT, especially with *A. l. atroparvus* of which the densely overcrowded 4th stage were reduced to the sensitivity level of 1st stage larvae. This effect was probably due to partial starvation which was evident in the smaller size of the larvae. The greater effect with *A. l. atroparvus* was probably due to their exclusively surface-feeding habit, whereas *A. stephensi* can feed also at the bottom.

Tests were also done with adult mosquitoes by the Busvine/Nash method. Results over a period of 2 years were consistent, indicating a stable susceptibility in the colonies. Tests conducted at different periods in the life of the adult females showed highest tolerance in the day of emergence which then declined somewhat until they obtained a blood meal, which effectively lowered susceptibility. In the next few days susceptibility increased until the next blood meal when the sequence was repeated. With advancing age, tolerance gradually declined. This pattern [found also by HADAWAY and BARLOW, this *Bulletin*, 1957, v. 54, 534] was evident in both species.

The results are compared with those of other workers.

J. R. Busvine

ALKAN, B. Versuche zur Bekämpfung von Stechmückenlarven in Reisfeldern bei Ankara in den Jahren 1947–1950. **[Tests on the Control of Mosquito Larvae in Rice-Fields near Ankara in 1947–50]** *Ztschr. f. Angewandte Entom.* 1957, v. 41, Pt. 4, 443–8. [Summary taken from *Rev. Applied Entom.* Ser. B. 1960, June, v. 48, Pt. 6, 104.]

Tests on the control of mosquito larvae in irrigated rice-fields were carried out near Ankara in 1947–50 with a number of synthetic insecticides that had been found in the laboratory to give 100 per cent. kill of larvae in 24 hours. Of the Anophelines known in Turkey, *Anopheles hyrcanus* (Pall.) and *A. sergentii* (Theo.) are reported as developing in rice-fields, and observations by the author showed that *A. maculipennis* Mg., *A. sacharovi* Favr (*elutus* Edw.) and *A. superpictus* Grassi occurred near them, the first two species in swamps and the last in flowing water. The Culicines concerned comprised mostly *Culex pipiens* L. and *C. hortensis* Fic. The two genera were usually present in about equal numbers. Rice is sown in about mid-May, and the larvae were present from the end of June or beginning of July to the end of September or beginning of October. Plots, mostly of about 600 sq. yards, were treated as soon as larvae appeared and again whenever the population increased, and the effect of treatment was assessed 1 and 4–7 days after each application and again on subsequent occasions. The treatments included the application of a dust containing 5 per cent. DDT, granules of 1 per cent. dieldrin on bentonite and briquettes containing 0·15 per cent. γ BHC in gypsum at rates of 0·12, 0·0375 and 0·42 oz. per sq. yard, respectively. The periods that elapsed, in days, before additional applications were needed and (in brackets) the percentage reductions obtained in numbers of Anopheline larvae as compared with untreated plots were 51 (91) for DDT, 45 (75) for dieldrin, and 39 (69) for γ BHC when the briquettes were applied where the irrigation water entered the fields and 34 (73) when they were distributed over the plots. There were no phytotoxic effects. Other treatments, though they sometimes gave kills that were as good or better, did not give quite such long periods of effectiveness

and presented, to a greater or lesser extent, difficulties in preparation of the material or in their application. In practice, granules and briquettes were preferable to dusts or liquid preparations. The probable cause of the incomplete control in the plots was continual carriage of mosquito larvae by flowing water from untreated to treated areas, so that treatment of much larger areas would be needed for eradication.

KYO, T. [**Morphological Observation on *Plasmodium inui* by means of Phase-Contrast Microscope**] *Japanese J. Parasit.* 1959, Oct., v. 8, No. 5, 759–74, 1 text-fig. & 63 figs. on 2 pls. [37 refs.] [In Japanese.] English summary.

The author describes the appearance of *Plasmodium inui* observed by phase-contrast microscopy of the blood and spleen of infected macaque monkeys. The trophozoites were rounded or oval, and contained numerous granules; they showed only slight amoeboid movement, though sometimes their mobility was increased. The gametocytes appeared to be motionless. The nucleus of the parasites was represented by a luminous body. Mature schizonts of "rosette" form resembled those of *P. vivax*: they were of irregular round shape and motionless; neither division of the nucleus nor liberation of merozoites could be observed.

The author believes that there is no segmentation of the "merocyte", nor penetration [of red blood cells] by merozoites in the peripheral circulation; he thinks that these phenomena take place in the tissues, and concludes that "the previous descriptions concerning erythrocytic life cycle [of malaria parasites] . . . need to be corrected and supplemented". *C. A. Hoare*

BOWMAN, I. B. R., GRANT, P. T. & KERMACK, W. O. **The Metabolism of *Plasmodium berghei*, the Malaria Parasite of Rodents. I. The Preparation of the Erythrocytic Form of *P. berghei* separated from the Host Cell.** *Exper. Parasit.* New York 1960, Apr., v. 9, No. 2, 131–6. [19 refs.]

The present investigation deals with the isolation of *Plasmodium berghei* from its host cell in order to compare some of its properties with those of the parasite occurring in the red cell.

The strain was maintained in rats and mice and infected blood obtained by cardiac puncture. Blood with a high percentage of reticulocytes was obtained as described [this *Bulletin*, 1954, v. 51, 537]. White cells were removed from the infected blood and red cells, infected to the extent of 90%, were isolated by the methods described [*ibid.*, 1956, v. 53, 1096, 1097]. Parasites were freed from red cells by means of antiserum from rabbits. Metabolic studies were carried out in buffered salt solution (saline A) or in saline with Na : K ratio, either 32 : 1 (saline B) corresponding to that in serum, or 1 : 7 (saline C) as occurs in the red cell, with the addition sometimes of reticulocyte extracts. Counts of the number of different type cells used in respiration experiments were made in stained or unstained preparations. Haemolysis was carried out in the respiration vessels so that the metabolic reactions of lysed and unlysed infected cells could be compared directly.

The separated parasites had a low degree of infectivity compared with intact infected red cells. These isolated parasites did not contain endogenous substrate and their rate of glucose catabolism was low, being enhanced by addition of saline C. Catabolism of glucose by free parasites in an extract of normal reticulocytes was similar to that in an intact cell but respiration was lower.

J. D. Fulton

MACDONALD, I. **The Interrelationship of Diet and Infection in the Production of Experimental Hepatic Fibrosis.** *J. Trop. Pediatrics.* London. 1960, June, v. 6, No. 1, 3–8, 3 figs. [13 refs.]

"Sub-threshold insults to tissues can summate and result in altered function." Thus, in protein malnutrition an intercurrent attack of gastro-enteritis may cause an acute accentuation in the malnutritional syndrome. WALTERS and WATERLOW in 1954 [this *Bulletin*, 1955, v. 52, 395] in a study of hepatic fibrosis among Gambian children, also postulated a dual aetiology, implicating the combined effects of moderate protein deprivation and endemic malaria.

The author has carried out an elegant and conclusive experiment on mice which he maintained on a diet known to cause hepatic fibrosis in rabbits. He then infected the animals with *Plasmodium berghei*. The diet, which comprised calcium caseinate 35·5%, sucrose 57·5%, dried yeast 2%, salts 5% and added vitamins A and D, was given *ad libitum*. The malarial infection, having been induced by the intraperitoneal injection of *P. berghei*, was controlled in some animals when 5% of the red cells had become parasitized, by intramuscular chloroquine in small doses; reinfection was induced whenever the infection died out.

When each animal died the liver was removed and weighed, a portion was set aside for histological examination and the remainder was desiccated. The fat content of the dry liver was then estimated, and the collagen in the dry, fat-free specimen was determined.

Groups of animals, treated as follows, constituted the experiment:—(i) experimental diet and malaria, (ii) normal diet and malaria, (iii) experimental diet and malaria plus chloroquine, (iv) normal diet and malaria plus chloroquine, (v) experimental diet and chloroquine, (vi) normal diet and chloroquine, (vii) experimental diet, (viii) normal diet.

From the table in which the results are set out, the following figures are extracted:

Group	Collagen in dry, fat-free liver, in gm./100 gm.		Mean liver lipid gm./100 gm.
	mean	SE of mean	
(i)	4·5	±0·93	12·1
(ii)	2·5	±0·45	14·4
(iii)	3·6	±0·57	16·4
(iv)	3·4	±0·72	8·1
(v)	2·1	±0·56	16·4
(vi)	2·7	±0·24	15·7
(vii)	3·1	±0·36	18·2
(viii)	2·0	±0·20	12·9

By an analysis of variance, the following conclusions appear to be justified:

(a) the experimental diet increases hepatic collagen;
(b) malarial infection alone increases hepatic collagen;
(c) the combination of malaria with the experimental diet causes a (maximal) increase in liver collagen;
(d) chloroquine plus malaria on a normal diet causes a slight increase in hepatic collagen, which is not seen in the case of the normal diet plus chloroquine: chloroquine therefore does not itself provoke collagen formation.

In sections impregnated with silver it is seen that whereas in the animals fed on a normal diet and infected with malaria there is some increase in the mid-zonal reticulum, in the malarious animals fed on the deficient diet mid-zonal fibrosis is more marked and is accompanied by an excess of reticulin fibres radiating from both the portal tracts and the central veins. These changes can be observed as early as 22 days after infection.

The author concludes that the combination of insults not only causes a much greater increase in collagen formation than either insult when administered alone, but this change takes place much more rapidly when both aetiological factors act in combination. There is evidence to support the view that such excessive collagen may not remain as a permanent scar, and the removal of part of the collagen produced may explain the lower collagen content of the livers of the mice fed on the experimental diet and subjected to malaria controlled with chloroquine, which lived twice as long as similar mice whose malaria was allowed to run its fatal course. *J. H. Walters*

Radacovici, Ecaterina, Iştan, T. & Dinculescu, M. Incercări de transmitere a parazitului malariei de rozătoare—*Plasmodium berghei*—la embrioni aviari. [**Attempts to transmit the Parasite of Rodent Malaria—*Plasmodium berghei*—to Avian Embryos**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1960, May–June, v. 5, No. 3, 277–83, 4 figs.

The English summary appended to the paper is as follows:—

"The authors confirm the results obtained by McGhee [this *Bulletin*, 1955, v. 52, 611] in the transmission of *Plasmodium berghei* from rodents to duck and goose embryos.

"Moreover, they were able, for the first time, to transmit the parasite to chick embryos."

Huff, C. G., Weathersby, A. B., Pipkin, A. C. & Algire, G. H. **The Growth of Exoerythrocytic Stages of Avian Malaria within Diffusion Chambers in Different Hosts.** *Exper. Parasit.* New York. 1960, Apr., v. 9, No. 2, 98–104, 1 fig.

The authors have made use of diffusion chambers based on a pattern described by Algire *et al.* (*J. National Cancer Inst.*, 1954, v. 15, 493) as a means of growing exo-erythrocytic stages of the avian malaria parasites, *Plasmodium gallinaceum* and *P. fallax*, within different hosts. The chambers were made by cementing cellulose ester membranes to lucite rings of two sizes, one of which

fitted inside the other. The maximum diameter of the outer ring was 17 mm. and the smaller diameter of the inner ring 10 mm.; each being 0·5 mm. thick. Cross-sectional views are given of 7 different types of chamber in which the pore size of the membranes was approximately 0·5 μ.

These chambers were planted within the various animals either intraperitoneally, intramuscularly or subcutaneously, and also in the yolk sac or on the chorioallantoic membrane of chick embryos. A typical experiment consisted of placing embryonic organs of chicks infected with *P. gallinaceum* in one of the above chambers in various sites in chickens for periods of 1–14 days. Some of the chicks became infected and this pointed to an imperfection of the chamber. In other experiments turkeys, ducks and chick embryos were used, and also mice for a total period of 3 to 21 days. Further tests were deemed necessary to determine the limit of pore size to prevent escape of parasites. The reactions of the different hosts to the implanted chambers varied widely, being more marked in chicks than in turkeys. The former host could encapsulate completely the chamber and limited the value of the method. It was proved that *P. fallax*, whose exo-erythrocytic stage does not infect mice, could survive and grow for 3 weeks in these porous chambers in this animal and thus allow study of different host parasite relationships as previously indicated (Huff, *J. Parasitology*, 1956, v. 42, 1). In some cases the contents of the chambers were more heavily infected than is generally the case in tissue.

The authors justifiably conclude that the use of porous chambers should prove of considerable help in the study of many parasitological problems.

J. D. Fulton

Rahm, U. & Kauffmann, M. Beeinflussung des Malaria-Verlaufes bei Kücken durch Tusche-Speicherung im RES. **[Effect of Indian Ink Blockade of the Reticulo-Endothelial System upon the Course of Fowl Malaria]** *Acta Tropica*. Basle. 1959, v. 16, No. 4, 302–30, 16 figs. [19 refs.]

According to previous investigations [this *Bulletin*, 1956, v. 53, 1208], the influence of high altitudes upon fowl malaria is due to stimulation of the reticulo-endothelial system (RES). In order to determine the exact part played by the RES in the course of infection with *Plasmodium gallinaceum*, various doses (3–78 mgm.) of Indian ink were injected intravenously into infected young chickens, and quantitative assays—as well as histological examination—of the spleen, liver and kidney were carried out with the view to ascertaining the granulopexic effect of this treatment. It was shown that the most striking effects were produced by blockade, rather than by stimulation of the RES. In the authors' view this is due, on the one hand, to the functional immaturity of the RES in young chicks, and, on the other, to the dual role of the macrophages as phagocytes and host cells for the exo-erythrocytic stages of the parasite. There are however definite indications that the functional state of the RES has a direct effect on the course of infection in birds.

The appearance of the blocked organs is shown in photomicrographs.

C. A. Hoare

TRYPANOSOMIASIS

*In this section abstracts are arranged as far as possible in the following order:—*African*—human, animal;* American*—Chagas's disease and other trypanosome infections. In each form the following order is followed:— epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control.*

Bloss, J. F. E. **The History of Sleeping Sickness in the Sudan.** *Proc. Roy. Soc. Med.* 1960, June, v. 53, No. 6, 421–6, (Sect. History of Med. 7–12.) 2 figs. [26 refs.]

The sleeping sickness area of the Sudan was in the South, bordering the French Sudan, the Congo and Uganda, and a special commission was appointed in 1905 to report on the situation. In 1910 considerable numbers of cases were found in the extreme south, and a large area was cleared as a segregation camp. A more serious outbreak occurred further west in 1918, and again a segregation camp was prepared, and watering-places and river-crossings were cleared of vegetation to control the tsetse flies.

Shortly afterwards a self-supporting settlement was created, and grain was imported into it, but the scheme had to be abandoned for lack of support from the local chiefs. Later the people were collected, not in villages, but along roads where clearings were made, and this plan succeeded because the powerful chiefs supported it. Inspection became easier, and more cases were found; between 1920 and 1929, 3,630 patients had been admitted, of whom 1,661 died. "In the course of the campaign against sleeping sickness the habits of the natives were transformed . . . the task of extirpating a disease had profoundly affected the life of a people."

Later the Symes block method of clearing for the control of *Glossina palpalis* was widely and successfully used, and in 1943 a proposal was made by the Director of Agriculture for development of a large area. By 1951, 48,000 families had been resettled, houses built, crops sown and rich harvests reaped in an area of 25,000 square miles "by gentle persuasion and, what is more important, quickly, cheerfully and freely by the Zande themselves".

Bloss writes that "Human sleeping sickness had been one of the major tropical epidemics and like the major epidemics of temperate climates it is important to realize that its control has depended, and still depends, on public health—environmental medicine—rather than on clinical medicine. There can be few diseases where it is necessary to have such a versatile and all-round knowledge of the vector, the people, their language and customs, the fauna, the flora, and the geography of the area".

He mentions that chemoprophylaxis was also used where indicated, and made control possible without the need for drastic restrictions. "Indeed modern methods of control make social and economic progress possible."

Charles Wilcocks

Morris, K. R. S. **Studies on the Epidemiology of Sleeping Sickness in East Africa. III. The Endemic Area of Lakes Edward and George in Uganda.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, May, v. 54, No. 3, 212–24, 1 fig. & 1 map. [18 refs.]

The area of some 1,500 square miles concerned in this study is an extension into Uganda of an old-established focus in the Semliki Valley in the Belgian

Congo. In 1910 investigation revealed an extensive epidemic around the Lake Edward area in Uganda. Control was difficult and in 1913–14 the inhabitants were moved to the Ruwenzori foothills where streams infested by *Glossina palpalis* were numerous, and in addition fishing areas in and near the lake and the Katwe salt trade were protected by clearings. The disease soon appeared in the new settlements but no systematic investigation was made until 1931 when it was found to be epidemic, though very mild. The outbreak was attacked by mass diagnosis and treatment, contact with fly was reduced by clearing the riverine vegetation and the provision of plantations for wood supplies in safe areas. In 1938 control ceased but in 1942 it was re-instituted because the incidence was rising again. Since then there has been no major trouble and only two tiny outbreaks in 1946 and 1953.

The change from endemic to epidemic conditions in 1910 was caused by increased activity and movement resulting from European administration. The incidence was almost confined to males engaged in canoe transport and fishing. The area into which the people were evacuated in 1913 was only some 12 by 3 to 4 miles, and expansion from it was limited by natural boundaries. The vegetation consisted of riparian fringing forest, the haunt of *G. palpalis*, and since game, reptiles and cattle were absent the fly was dependent on man for its food supply. Thus both human and fly populations were concentrated into a restricted habitat, and close and regular contact between man and fly resulted. The disease commonly infected women and children. In the inter-epidemic periods the disease persisted, in spite of a low incidence of apparent infection, because it was so mild that those infected were not incapacitated and not diagnosed, and as a result of relapses and re-imported infections.

[Previous papers in this series are reviewed in this *Bulletin*, 1960, v. 57, 106 and 562.] *T. H. Davey*

Inoki, S. & Matsushiro, A. **Relationship between Kinetoplast Elimination and Para-Rosaniline Resistance in** *Trypanosoma gambiense*. [Correspondence.] *Biken's J.* Osaka. 1959, Dec., v. 2, No. 4, 371–4, 3 figs.

Bursell, E. & Glasgow, J. P. **Further Observations on Lake-Side and Riverine Communities of** *Glossina palpalis fuscipes* **Newstead.** *Bull. Entom. Res.* 1960, Apr., v. 51, Pt. 1, 47–56, 3 figs. [11 refs.]

Previous work [this *Bulletin*, 1955, v. 52, 132] has suggested that riverine communities of *Glossina palpalis fuscipes* were more hungry than lake-side communities. Puparia of this species were collected from the upper Kuja river and from Waturi on the shore of Lake Victoria. Both localities are in the Nyanza Province of Kenya and are 25 miles distant from each other. The riverine puparia were larger than those from the lake-side, and so also were the flies that emerged from the puparia. The larger flies did not contain a larger proportion of fat per body weight. Non-teneral flies captured in the river area were slightly larger than non-teneral flies captured by the lake shore, but the difference in size was less than half that shown between the two populations in the puparia and newly-emerged flies. This difference, it is suggested, may be due to elimination of the smaller flies in the lake shore community.

During the dry season the size of flies and puparia showed a progressive decrease, suggesting that the populations were then short of food. At this time a high proportion of non-teneral males were captured and it is suggested that this may be a useful indicator of the state of nutrition.

B. R. Laurence

SAUNDERS, D. S. **Determination of Physiological Age for Female** *Glossina morsitans*. [Correspondence.] *Nature*. 1960, May 21, v. 186, 651, 2 figs.

In the past year or so there has been much interest in the possibility of determining the age of mosquitoes from the number of follicular relics present in the follicular tubes [this *Bulletin*, 1958, v. 55, 713 ; 1959, v. 56, 245, 510], each relic being in the form of cellular debris in a small dilatation of the tube and representing the site of a former egg follicle. If the duration of each reproductive cycle is known, the means are at hand to estimate the insect's age.

The principle is here investigated for *Glossina morsitans* in the laboratory in flies obtained from puparia sent from Africa and suitably fertilized and nourished. Each of the two ovaries contains *two* ovarioles. Only one egg matures at a time, the sequence being: first egg from right ovary; second egg from left ovary; third egg from right ovary; fourth egg from left ovary, and so on. Immediately after ovulation of an egg into the uterus, the follicle from which it erupted is saccular. But a distinct small dilatation containing follicular debris is not subsequently formed from it, so that persisting bead-like " follicular relics " as in mosquitoes are not available for ageing purposes; but there persists a residual distension (or stump) of the base of the follicle which is still evident once the sac formation has subsided. The age of a tsetse could be estimated up to 40 days (at 26° C.). Thus, since the sequence of ovulation was constant, the actual follicle currently developing could be used as a measure of time, the fourth egg ovulating after 40 days. Younger flies showed the first egg ovulating at 8 to 9 days and the second and third at 10-day intervals. Larval development could allow of refinement in calculating age. It is apparently impossible to calculate beyond 40 days, *i.e.* beyond the age at which the fifth egg would develop, involving the right ovary for the third time.

Observations of this nature on wild-caught tsetse could, it is suggested, be valuable in assessing the age of tsetse, but within the limits specified.

D. S. Bertram

LAPEYSSONNIE, L. Deuxième note concernant un cas exceptionnel de trypanosomiase. Parasitémie observée depuis 21 ans sans signes cliniques appréciables chez une malade traitée inefficacement pendant les dix premières années. [**Second Note about an Exceptional Case of Trypanosomiasis. Parasitaemia observed during 21 years without appreciable Clinical Signs in a Patient treated ineffectively during the First Ten Years**] *Bull. Soc. Path. Exot.* 1960, Jan.–Feb., v. 53, No. 1, 28–32, 3 figs.

The patient was a young woman of Togoland. In 1938, when 4 years old, she had been found to have trypanosomiasis. In 1948 [this *Bulletin*, 1949, v. 46, 533] she was described as having infections of blood and lymph nodes in spite

of treatment with all the known trypanocides including pentamidine, but her cerebrospinal fluid [CSF] was normal and there were no clinical signs of ill effects from her infection. In 1949 the lymph juice and bone marrow were found to contain numerous trypanosomes; the trypanosomes were stumpy, stained deeply with Giemsa, and appeared to have no free flagellum. Various animals (mice, guineapigs, monkeys) were inoculated but did not become infected. The patient's health was excellent and the CSF was normal. In 1959 the woman was examined again and the findings were reported to the author. She was still quite healthy and had become the mother of two children. The cervical lymph nodes were palpable and trypanosomes were found in her blood on 6 separate occasions, 21 years after the first diagnosis. Drawings are reproduced of the trypanosomes as they appeared in 1949. [They seem to resemble *Trypansoma congolense* rather than *T. gambiense* although they are broader than *congolense*.] They appear to be resistant to drugs and perfectly tolerated by the host (woman). *F. Hawking*

APTED, F. I. C. **Nitrofurazone in the Treatment of Sleeping Sickness due to *Trypanosoma rhodesiense*.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, May, v. 54, No. 3, 225–8.

Nitrofurazone in addition to its other therapeutic uses has been found to be of value in the treatment of trypanosomiasis [this *Bulletin*, 1956, v. 53, 31; 1957, v. 54, 136; 1958, v. 55, 135 and 136]. Its particular promise in this connexion lies in its action on some infections resistant to all the other accepted trypanocidal drugs, including Mel B. The most obvious toxic effect of the drug is a peripheral neuritis.

In previous experimental work it has been reported to be less effective against *Trypanosoma rhodesiense* than against *T. gambiense* infections. 9 patients with *T. rhodesiense* infections were treated by the author with nitrofurazone given orally. The dosage was from 1·5 to 2 gm. daily, divided into 4 doses, and continued over periods of 5 to 7 days. After a week this course was repeated; in some of the cases it was similarly repeated on a further 2 occasions. The gross dosages given to these particular patients therefore ranged from 170 to 583 mgm./kgm. body weight. One patient following a single course of 255 mgm./kgm. without other treatment enjoyed a 2-year "cure"; but a similar dosage failed in other patients; and, again, yet others resisted a dosage 3 times that amount. Nevertheless, of the 9 patients treated with nitrofurazone, with or without combination with Mel B, 4 who otherwise certainly would have died have remained alive and well. The lives of others have been considerably prolonged by its use, though the final outcome in these is doubtful. Variation in the individual responses to treatment with the drug adds to the difficulty of assessment of its value in so small series of cases, and the subsequent period of observation also has been short. It is quite clear, however, that nitrofurazone merits further study as a trypanocide by virtue of its proven value as such.

A. R. D. Adams

DAVIES, J. B. **Use of Dieldrin in the Control of *Glossina palpalis* (R-D) in Nigeria.** [Correspondence.] *Nature*. 1960, July 2, v. 187, 84–5.

Spraying riverine vegetation with 5% DDT suspension gives satisfactory control of *Glossina tachinoides* in the dry savannah zone of Nigeria. Where drought is less intense and dews fall at night, this measure has not been so effective even if repeated 5 times at 2-week intervals. In such an area, broken up by many small but mostly perennially flowing rivers, each supporting forest vegetation to a width of 5 to 500 yards on either bank and a reasonably high population of *G. palpalis* and *G. tachinoides*, a length of 4·5 miles of river was isolated by bush clearance and sprayed with dieldrin emulsion diluted on the spot to 4% concentration. Spraying was concentrated on all vegetation living and dead up to 4 feet from the ground, throughout the width of the riverine vegetation. The effect was an immediate disappearance of flies; fly rounds gave consistently negative results until they were discontinued a year later. The cost of spraying was £41 a mile. DDT spraying (5 applications) would have cost £50 10s. 0d. a mile, and partial clearing £100 to £200 a mile. A longer stretch of river has since been sprayed with dieldrin, with encouraging results. [See also DAVIES, this *Bulletin*, 1959, v. 56, 133.] *B. B. Waddy*

RHODESIA, NORTHERN. **Ministry of Land & Natural Resources. Dept. of Veterinary and Tsetse Control Services. Annual Report for the Year 1959** [SWAN, J. F. C., Director of Veterinary & Tsetse Control Services] **Part IV. Tsetse Control** (pp. 5–13). 21 pp. 1960. Lusaka: Govt. Printer. [2s. 6d.]

Tsetse threaten human settlement from two main flybelts in Northern Rhodesia, which together cover some 90,000 square miles and have a fly front about 5,000 miles long. One of these belts extends along the Luangwa basin and the Lunsemfwa river and its tributaries, the other stretches from near the Copper Belt in the north to Kalomo in the south, almost reaching the Zambesi. Outside these belts carried fly are a serious problem which has been met by amending the Tsetse Control Ordinance to cover not only areas within the fly belts but also areas subject to temporary infestation with carried fly. By this Ordnance travellers and traffic are confined to specified routes on which disinfestation is practised and where introduced fly will not menace livestock. The summary of the Chief Entomologist's report indicates the very wide range of control measures employed.

In the Central Province the position has improved and also in the Southern Province except in the Chirundu area where fly are increasing, probably carried in by traffic from Southern Rhodesia. Fly are also infiltrating along a newly-established power line cut through thicket previously impenetrable to *Glossina morsitans*. In Luapula Province discriminative clearing has proved ineffective by itself and game elimination is to be associated with it. In the North-Western Province trypanosomiasis in the scattered population can only be controlled by redistribution and concentration of the people. *G. palpalis* near Lake Tanganyika has been controlled by insecticides, particularly dieldrin. In Barotseland fly potential is building up and an entomologist is being sought to investigate it. Sleeping sickness cases numbered 110 in the year and came from all known endemic foci; in two districts, Mpika and Kasempa, the situation has deteriorated. *T. H. Davey*

LAMBELIN, G., ECTORS, F., VAN VAERENBERGH, R. & MAMMERICKX, M. Sensibilité du buffle d'Asie aux principales maladies à protozoaires du bétail au Congo belge. Essais expérimentaux et observations cliniques. [**Experimental and Clinical Studies on the Susceptibility of the Asian Buffalo to the Principal Protozoal Diseases of the Cattle in the Belgian Congo**] *Ann. Soc. Belge de Méd. Trop.* 1960, Feb. 29, v. 40, No. 1, 189–97.

The English summary appended to the paper is as follows:—

"The Asiatic domestic buffalo is very susceptible to *Theileria parva* and *Trypanosoma vivax*. On the contrary, it endures better the infection caused by *Trypanosoma congolense* and it seems to resist quite well *Piroplasma bigeminum* and *Anaplasma marginale*.

"Further researches, especially concerning the last called parasite, are necessary."

GAIKHORST, G. **The Presence of *Trypanosoma cruzi* on the Island of Aruba and its Importance to Man.** *Trop. & Geograph. Med.* Amsterdam. 1960, Mar., v. 12, No. 1, 59–61.

At a meeting of the Netherlands Society of Tropical Medicine in November 1958, VAN THEIL described the finding of *Trypanosoma cruzi* in triatomid bugs in Aruba, Netherlands Antilles (*Trop. Geograph. Med.*, 1959, v. 11, 189). Since the number of clinical cases of Chagas's disease is small in proportion to the number of latent infections—even in countries like Brazil where the disease is so common—the present author surveyed 2,243 sera from inhabitants of Aruba, to determine whether serological evidence of *T. cruzi* infection was present.

He used a complement-fixation reaction with an extract of cultivated trypanosomes (originally isolated from a triatomid bug) as antigen. Full details are given of the preparation of the antigen. Suitable positive control sera were included in the tests.

All sera were negative so that not even subclinical infections were detected. It is concluded that human infection with *T. cruzi* does not occur—or, if it does, occurs rarely—in Aruba. Possible explanations of this are that: (1) local triatomids exist principally in animal dwellings and rarely penetrate human habitations, (2) the local strain has little virulence for man. Work is being pursued on the question of the animal reservoirs from which triatomids are infected in Aruba: at present, this is unknown. *H. J. O'D. Burke-Gaffney*

ACUÑA F., Inés & MASSA, G. Relación entre vitamina C y el condrioma en el *Trypanosoma cruzi*. [**Relation between Vitamin C and the Chondriome in *Trypanosoma cruzi***] *Rev. Servicio Nacional de Salud*. Santiago. 1958, Dec., v. 3, Nos. 3/4, 445–53.

It is known that the cytoplasm of *Trypanosoma cruzi* contains an abundant chondriome in granular form, while cytologists have shown that it is rich in ascorbic acid and probably plays an important role in cellular respiration. It has also been demonstrated that laboratory animals suffering from vitamin C deficiency are refractory to infection with *T. cruzi*.

In order to study the effect of ascorbic acid upon the chondriome of *T. cruzi in vitro*, the trypanosomes were cultivated with the addition to the medium of various amounts of this vitamin, and the appearance of the chondriome was examined by phase microscopy and by staining with Janus green. It was found that the addition to the culture medium of 5 mgm. ascorbic acid produces enlargement of the chondriome and an increase in the number of flagellates.

C. A. Hoare

HARINGTON, J. S. **A Simple Apparatus for the Artificial Feeding of *Rhodnius prolixus* (Hemiptera, Reduviidae).** *Parasitology*. 1960, May, v. 50, Nos. 1/2, 273–7. [10 refs.]

Thin Durex rubber was used as a membrane through which to offer various diets to all stages of *Rhodnius prolixus*. The diet was kept at 38°–40°C. (for the first three instars) and as high as 44°C. (for the later stages), these being temperatures giving best feeding results.

Sterile bugs were much more reluctant to feed than normal bugs. The latter showed a considerable range in acceptance of unusual diets, even although some were sufficiently unfavourable to cause death within 24 hours, or longer, after the meal. An account is given of these findings for normal bugs only. Young bugs fed more readily than older ones on the unusual diets offered. Distilled water and aqueous solutions of glycine or ascorbic acid were not accepted by the bugs; they probed well through the membrane but would not suck. Marmite solutions up to 10% in water, Ringer's solution, cow's milk, oxalated horse blood, citrated rat blood, whipped ox blood and horse serum were all quite readily ingested. Mortalities were high within 24 hours with Marmite, Ringer's and cow's milk. Stored oxalated horse blood was fatally toxic within 21 days. On occasions, bugs fed on serum collapsed for several hours after the meal. They recovered, although later on beyond the third stage they died, sometimes deformed. Feeding and growth was successful only on freshly drawn blood (citrated rat, or oxalated horse, or whipped ox blood).

Although contact of the proboscis or antennae with water does not repel the bugs, contact of their tarsi, particularly the front legs, with water repelled bugs from a feeding surface. *D. S. Bertram*

HARINGTON, J. S. **Studies on *Rhodnius prolixus*: Growth and Development of Normal and Sterile Bugs, and the Symbiotic Relationship.** *Parasitology*. 1960, May, v. 50, Nos. 1/2, 279–86, 1 fig. [16 refs.]

No adults were obtained in several hundreds of *Rhodnius prolixus* deprived by egg sterilization of their gut symbiont *Nocardia rhodnii* and subsequently reared under sterile conditions. Differences between sterile and normal bugs became apparent at the blood meal of the first stage larvae, sterile bugs ingesting less blood (3·75 mgm. blood per bug) than normal bugs (4·4 mgm. blood per bug). Earlier workers in this field of study obtained normal growth and moulting to the third, fourth, or even fifth larva stage. In the present work, sterile larvae weighed less and moulted sooner than the corresponding normal bugs, and their moulting at the fourth stage (when mortality was almost complete) was spread erratically over 19 to 46 days. Only 6 larvae successfully

moulted into the fifth stage; 3 of these died while moulting to adults and showed deformity [this *Bulletin*, 1954, v. 51, 35]. The author inclines to the view that, in sterile bugs, growth and moulting for the earlier larval stages is possible because of necessary substances—and these may be vitamins—available from the egg itself but not in sufficiency to achieve complete development to adult stage.

In subsidiary work, oxytetracycline and also aureomycin and chloramphenicol inhibited growth of *Nocardia rhodnii in vitro*. Symbionts of *Triatoma* were inhibited—in work by others [*ibid.*, 1955, v. 52, 21]—only by oxytetracycline. Ingestion of succinylsulphathiazole, offered in serum, by normal *R. prolixus* suggested that elimination of the symbiont was effective at least for many days; moulting failed.

Emphasis is given to the fact that normal *R. prolixus* usually harbour only *N. rhodnii* with occasionally also another organism, *Streptococcus liquefaciens*. *Triatoma infestans* may also be infected only with *N. rhodnii* but often with several other organisms (*Bacterium*, *Corynebacterium*, *Staphylococcus* and *Streptomyces* spp.) [*ibid.*, 1956, v. 53, 427]. Comparative studies of the significance of symbiont infection in different species of bug need to take account of these differences in gut flora. *D. S. Bertram*

LEISHMANIASIS

In this section abstracts are arranged as far as possible in the following order:—visceral, cutaneous, muco-cutaneous.

SYMMERS, W. St. C. **Leishmaniasis acquired by Contagion. A Case of Marital Infection in Britain.** *Lancet*. 1960, Jan. 16, 127–32, 4 figs. [37 refs.]

In this paper there is a record of an astonishing case and of 4 others of interest. The first was that of a woman aged 38 who developed an irritable papule behind the vaginal orifice and after a month during which it enlarged and ulcerated the lymphatic nodes in the groin became enlarged. Syphilis was diagnosed and a Wassermann reaction, performed by a person without experience of the test, was reported positive. She was treated with penicillin and developed an erythematous rash, and a Wasserman reaction, repeated at this time, was positive; the Kahn test done then for the first time was negative. The vulvar sore continued to enlarge in spite of therapy and a dark ground examination was only now carried out and was reported on as negative. The patient and husband denied having extramarital sexual intercourse but as the husband had no genital lesions, he doubted his wife's truthfulness and left home. Inconsistency between the clinical findings and a diagnosis of syphilis, however, led to a biopsy of the lesion now being done, 18 weeks after the

patient first noticed it. Chronic inflammatory changes and Leishman-Donovan bodies were found. The latter were also now found in a dark ground examination and the technician who had carried out the original examination realized that they had been present at that examination also but he had "not drawn anyone's attention to them because he had only been told to look for treponemas".

The patient had never been out of the British Isles, but on considering ways in which she had acquired the infection it was recalled that her husband had had kala azar in the Sudan and East Africa in 1941 and had been only erratically treated owing to the exigencies of war in which he had been taken prisoner. He had developed typical post-kala-azar dermal leishmaniasis in 1945 but after treatment then had been free from all symptoms. He married in 1953 and the wife's ulcer developed in 1955. Examination of the husband at this time revealed the presence of splenic, liver and generalized lymph-node enlargement and biopsy of a lymph node revealed Leishman-Donovan bodies. Both the man and the woman responded satisfactorily to routine treatment and have re-established their home.

The rash which occurred during the woman's penicillin treatment and which was thought to be syphilitic was evidently a reaction to the penicillin to which she has become sensitive and her Wassermann reaction has been shown to become positive whenever a penicillin reaction is provoked.

One of the other 4 cases described was of cutaneous leishmaniasis in a woman who had 5 weeks earlier spent a camping holiday in the South of France but had otherwise never been out of England.

The remainder of the paper consists of a review of the relevant literature with which readers of this *Bulletin* will be familiar. *A. W. Woodruff*

See also p. 1108, DAOUD & SCHWABE, **Sensitivity of Lebanese and Syrians to Toxoplasmin and to a Similar Antigen prepared from** *Leishmania tropica.*

GHOSH, B. K., HALDAR, D. & CHATTERJEE, A. N. **Effect of Nystatin on the Metabolism of a Protozoal Organism,** *Leishmania donovani.* [Correspondence.] *Ann. Biochem. & Exper. Med.* Calcutta. 1960, Feb., v. 20, No. 2, 55–6.

The discovery of nystatin, an antibiotic produced by *Streptomyces noursei,* was described by BROWN and HAZEN (*Trans. New York Acad. Sci.*, 1957, v. 19, 448). It has antifungal properties and shows some activity against *Leishmania donovani* [this *Bulletin*, 1960, v. 57, 111]. The present authors have examined its activity against this parasite by the methods described [*ibid.*, 1960, v. 57, 460]. Because of the instability of the drug in solution it was prepared daily in propylene glycol. The substance was found to inhibit some metabolic activities of the organism to a high degree in concentration of 10 μgm. per ml., in presence or absence of a number of substrates. The inhibition produced was not reversible. Endogenous glycolysis was however not affected by nystatin, whereas fixation of carbon dioxide by cell suspensions was inhibited [*ibid.*, 1960, v. 57, 572]. The substance brought about marked morphological changes in the organism. The mechanism of action is being investigated.

J. D. Fulton

SEN GUPTA, P. C. & CHATTERJI, A. **Histopathology of the Spleen in Drug-Resistant Kala-Azar.** *J. Indian Med. Ass.* 1960, Feb. 1, v. 34, No. 3, 81–4, 6 figs. on pl. [16 refs.]

The results are described in this paper of histopathological study of spleens removed from 4 patients with kala azar who had not been cured by repeated courses of antimony and aromatic diamidines. The duration of the disease prior to splenectomy, which was carried out as part of therapy, varied from 4 to 5 years.

The spleens weighed between 3 and 5 kgm., they were firm and there was slight to moderate thickening of their capsules. Special histological features found were (a) leishmanial granulomata consisting of giant cells or epitheloid or histiocytic cells with or without leishmaniae, surrounded by masses of plasma cells and some lymphocytes; (b) evidence of reactive hyperplasia of occasional lymphoid follicles though most of these were atrophic; (c) haemosiderotic nodules and pigment; (d) haemopoietic foci.

In the discussion it is pointed out that the response of the human host to leishmanial infection is proliferation and accumulation of histiocytes, and the presence of granulomata in the spleen in these cases is additional evidence of this process. The reactive hyperplasia in a few Malpighian corpuscles in the series is possibly a compensatory phenomenon. The haemosiderotic nodules indicated organization of haemorrhage from splenic arterioles with formation of fibrous tissue incorporating the haemosiderin and calcium. No doubt these were caused by the long-standing congestion in the spleen in these drug-resistant cases. The haemopoietic foci in the spleen were probably the result of inadequate marrow haemopoiesis. [They provide a powerful argument for counselling very careful selection of such patients for splenectomy.]

A. W. Woodruff

DI STEFANO, F., PANARA, B. & PIETRANGELI, E. La leishmaniosi cutanea in Abruzzo nel decennio 1947–1956. [**Cutaneous Leishmaniasis in Abruzzo in the Period 1947–1956**] *Ann. d. San. Pubblica.* Rome. 1959, Nov.–Dec., v. 20, No. 6, 1243–60, 5 figs. [Numerous refs.] English summary (9 lines).

In the Abruzzi, visceral leishmaniasis was first reported in 1927, and oriental sore in 1933: the authors have studied the incidence of the latter disease in this region of Italy during the 10 years 1947–1956. The territory affected is on the Adriatic coast, involving almost the entire province of Teramo and parts of the provinces of Chieti and Pescara. They found evidence of considerably increased endemicity during and soon after World War II. Only some 4–9 cases were being notified yearly in pre-war years, but in 1946 259 cases were reported in this region and only 32 other cases from the rest of Italy. In the following year, centres for the diagnosis and treatment of the disease were established in each of these 3 Abruzzi provinces. These measures proved so successful that by 1952 the Pescara centre was adequate by itself to deal with all cases and the other two centres closed down.

The authors briefly review the activities of these three centres and tabulate

their findings and results, involving a total of 7,209 cases of cutaneous leishmaniasis. Only 11 cases of visceral leishmaniasis were diagnosed in the same period. Children up to 14 years of age made up about half the number of cases. The incidence of cutaneous leishmaniasis in the Abruzzi region made up some 30% of all the cases notified in Italy during these 10 years of 1947–56.

62% of the lesions were found on the face and 35% on the limbs, distally as a rule. The authors touch on the morphology of these lesions, treatment by atebrin and glucantime, modes of transmission and measures of controlling the disease. The reduction in incidence should not be mistaken for eradication and it is essential that cases should continue to be looked for and treated when found. *J. Cauchi*

ROTBERG, A. Leishmanides liquenoides e hipocromicas. [**Lichenoid and Hypochromic Leishmanids**] *Rev. Asoc. Med. Argentina.* 1960, Apr., v. 74, No. 4, 190–93, 3 figs. [12 refs.]

The English summary appended to the paper is as follows:—

"A 34 years old Negro woman, with lesions and scars of American Tegumentary Leishmaniasis since the age of 14, showed in the last 5 years, several outbreaks of papular lichenoid and hypochromic lesions on the dorsa of her hands and forearms and hypochromic areas on her forehead and nose, bordered by papules, in which no leishmanias were found. The outbreaks seemed to be caused by the ingestion of alcohol, sun exposure, puerperium and occurred once during the specific treatment; the hypochromic patches disappeared during the remissions of the papular eruptions, which were diagnosed as 'leishmanids'. The simple macular hypochromic areas are considered an unusual feature, as compared with the frequent depigmentation of the 'dermal leishmanoid' observed in cases of Kala-azar."

FEVERS OF THE TYPHUS GROUP

In this section abstracts are arranged as far as possible in the following order:—general; louse-borne typhus, flea-borne typhus, mite-borne typhus; rickettsialpox; tick-borne typhus; Q fever, other rickettsial diseases.

ČERVENKA, J., BERTAN, J. & SUTORISOVÁ-STOLZOVÁ, M. Menšia epidémia škvrnitého týfu z prípadu Brillovej-Zinsserovej choroby v zavšivenom prostredí. [**A Small Epidemic of Typhus Fever from a Case of Brill-Zinsser's Disease in an Environment infested with Lice**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1960, v. 9, No. 3, 148–55, 3 graphs. [13 refs.] English summary.

In the winter of 1953–54 an epidemic of typhus occurred near Bratislava, with 20 patients, 17 of whom were gypsies. The outbreak was preceded by a

mild illness in a gypsy who had suffered from typhus 4 years previously, and which was diagnosed as Brill's disease. This patient was regarded as the source of the infection, since the area had been free from epidemic typhus for some years. The disease in the other patients pursued a typical course, and they all recovered after treatment with chloramphenicol and tetracyclines. The epidemic was brought to an end by the prompt enforcement of public health measures. The authors draw attention to the danger of sporadic cases of typhus giving rise to epidemics in environments with unsatisfactory hygienic conditions. *D. J. Bauer*

KRASNIK, F. I. **The Epidemiological Importance of Patients with Sporadic Typhus.** *Problems of Virology*. London. 1959, v. 4, No. 4, 105–10, 2 figs.

Rickettsia prowazeki was isolated from 20 out of 140 typhus patients (sporadic cases) by feeding lice on their blood during the febrile stage of the disease. The highest proportion of successes (14 isolations in 58 attempts, or 24%) was obtained by allowing 1-day-old louse larvae to feed on patients on 2 consecutive days; the larvae were then fed on [?blood from] a donor and a sample examined microscopically after 8 to 10 days; if no rickettsiae were seen in intestinal smears, suspensions of the remaining larvae were fed to fresh larvae through a skin membrane, these larvae being examined later for rickettsiae. The majority of isolations (15 out of 20) were made on the 6th and 7th days of the disease; no isolations were made after the 8th day, by which time antibodies were detectable in the serum. It is concluded that sporadic and mild cases of typhus can be a real epidemiological danger under unfavourable sanitary conditions [a conclusion which it is surprising to see presented with any implication of novelty]. *R. S. F. Hennessey*

PSHENICHNOV, A. V., RAIKHER, L. I. & KOSTROMINA, E. E. **Possible Errors of Method in Work on the Detection of Minimal Amounts of Typhus Rickettsias.** *Problems of Virology*. London. 1959, v. 4, No. 2, 104–6. [Translated from Russian.]

Highly sensitive methods of detecting rickettsiae (*e.g.* by feeding louse larvae on test material through a skin membrane) increase the chances of isolating these organisms from sources other than those under investigation. The authors have recovered *Rickettsia prowazeki* from the air of a box in which infected lice were being fed on a rabbit, from normal lice incubated together with infected lice under conditions where rickettsiae could only have been transferred in air or dust, and from lice fed on the blood of patients who were not infected with *R. prowazeki*. They also isolated *R. prowazeki* from "ectroparasites" [ectoparasites] collected from infected guineapigs. These findings point to the possibility of accidental recovery of rickettsiae disseminated in the external environment and hence to "the need to insist on strict conditions being observed in experiments in which questions of principle regarding the pathogenesis of present-day typhus are decided on the basis of detection of the organisms". *R. S. F. Hennessey*

WEISS, E. & DRESSLER, H. R. **Centrifugation of Rickettsiae and Viruses onto Cells and its Effect on Infection.** *Proc. Soc. Exper. Biol. & Med.* 1960, Apr., v. 103, No. 4, 691–5. [14 refs.]

Cultures of chick embryo entodermal cells were readily infected with *Rickettsia prowazeki, R. burneti,* psittacosis virus and trachoma virus when tubes containing the cultures were centrifuged at 1,600–1,800 g for 1 hour at 20°C. after the rickettsial or viral suspensions were added. It was estimated that centrifugation enhanced the infection of cells with *R. prowazeki* about 10,000-fold, with psittacosis virus about 100-fold, and with trachoma virus at least 10-fold. Some enhancement of infection with *R. burneti* was also obtained. Centrifugation increased infection of cultured human skin cells with psittacosis virus at least 100-fold. It is concluded that the centrifugation procedure offers practical advantages in simplicity and efficiency, producing consistent results which closely resemble those obtained in eggs.

R. S. F. Hennessey

BOVARNICK, Marianna R. & SCHNEIDER, L. **The Incorporation of Glycine-1-C^{14} by Typhus Rickettsiae.** *J. Biol. Chem.* 1960, June, v. 235, No. 6, 1727–31. [18 refs.]

"Typhus rickettsiae can incorporate glycine-1-C^{14} maximally only in the presence of at least 0·13 M potassium ion. Reduction of the total solute concentration or substitution of even a fraction of the K salts by Na salts or by sucrose greatly reduces the uptake. Mg^{++} also is required and Mn^{++} further stimulates the uptake. A mixture of all the naturally occurring amino acids is necessary for maximal uptake of glycine and omission of any one of the three single amino acids tested reduces glycine uptake to a value almost as low as that found on omission of all.

"The incorporation of glycine is inhibited completely by KCN, dinitrophenol, and chloramphenicol.

"There is evidence that both externally added and internally generated adenosine 5′-triphosphate are required for incorporation of amino acids by rickettsiae."

PSHENICHNOV, R. A. **The Use of Radioactive Radiation for the Preparation of Rickettsial Antigens.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 3, 149–52. [Translated from Russian.]

Suspensions of *Rickettsia prowazeki* and *R. quintana* which received a dose of 5,000,000 r of gamma radiation from a cobalt source with a flux of 21,000 r per minute were completely inactivated without loss of specific titre or change in anticomplementary activity in the complement-fixation test, and behaved satisfactorily in the agglutination test. The irradiated suspensions were effective in producing immunity in guineapigs. In contrast, rickettsial suspensions exposed to 0·2% formalin did not become sterile until the 14th day of contact, were more anticomplementary, and caused more marked reactions on intradermal injection. These results "warrant the conclusion that the sterilization

of antigens by irradiation can be used for the preparation of rickettsial and virus antigens". *R. S. F. Hennessey*

FRYGIN, C. Aktywność serologiczna antygenu rozpuszczalnego *R. prowazeki*. [**Serological Activity of the** *R. prowazeki* **Soluble Antigen**] *Med. Dośw. i. Mikrob.* Warsaw. 1960, v. 12, No. 2, 167–74, 4 figs. [13 refs.] English summary.

Soluble antigen was prepared from a formalin-inactivated saline suspension of yolk sacs infected with *Rickettsia prowazeki* by low and high speed centrifugation, followed by resuspension in 1/5 volume saline and treatment with 1½ volumes of ether at 4°C. for 6–7 hours; the aqueous phase was then removed and extracted again with ether for 2–3 hours and subjected to high speed centrifugation. The supernatant fluid contained the soluble antigen, and was concentrated 10-fold by exposure to a current of hot air. It contained 0·4 mgm. of nitrogen per ml., and gave no precipitation or fixation of complement with antiserum to normal yolk sacs, and was therefore free from host components. The titres in antigenic units per ml. of 3 batches of the antigen were 339, 410 and 525 respectively. Soluble antigen treated with 0·2*N* NaOH at 100°C. for 30 minutes sensitized sheep red cells to agglutination by specific antisera in dilutions up to 40, and untreated antigen reacted with the antisera in capillary precipitation tests to a titre of 2–4. The antigen formed 2 lines of precipitate in gel diffusion tests. *D. J. Bauer*

FOLIGUET, J. M. De l'interprétation à donner au séro-diagnostic des rickettsioses par la technique de micro-agglutination de P. Giroud, en particulier, chez les vaccinés récents et anciens. [**The Interpretation of Serological Micro-Agglutination Tests (Giroud) in Rickettsial Diseases, particularly after Vaccination**] *Bull. Soc. Path. Exot.* 1960, Jan.–Feb., v. 53, No. 1, 72–82. [15 refs.]

The results of micro-agglutination tests on sera collected at various times from military personnel who had received killed anti-typhus vaccine (Durand-Giroud) showed that for a period up to 1 year after vaccination it would be unjustifiable to take as presumptive evidence of active infection titres below 1 in 640 for *Rickettsia prowazeki* and below 1 in 320 for *R. mooseri*; a rise and fall in titre, and a distinct fall in response to antibiotic therapy, should be observed. After 1 year, agglutinin levels of 1 in 320 and 1 in 160 for *R. prowazeki* and *R. mooseri* respectively could be accepted as indicative of infection. Some reserve would still have to be exercised in interpreting results, as agglutinins formed in response to vaccination may be increased by non-specific factors. *R. S. F. Hennessey*

IABLONSKAIA, V. A. **The Diagnostic Value of the Haemagglutination Test in Typhus.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 5, 137–42. [Translated from Russian.]

MEL'NIKOV, L. A. **The Serological Diagnosis of Rickettsioses of the Typhus- and Tick-Borne Spotted Fever Group by the Haemagglutination Method. II. The Specificity of the Reaction.** *Problems of Virology.* London. 1959, v. 4, No. 3, 10–14. [Translated from Russian.]

Haemagglutination tests on sheep red cells sensitized with antigens from *Rickettsia prowazeki*, *R. mooseri*, *R. conori*, *R. sibiricus* and *R. murinus* were performed with sera from 60 typhus patients, 15 patients with vesicular rickettsiosis [tick-borne spotted fever], 80 healthy persons, and 51 patients suffering from various infectious diseases (including 6 with Q fever). Unspecific haemagglutination was observed with 18–25% of sera up to a titre of 1 in 160. When titres below 1 in 250 were disregarded, not a single unspecific reaction was obtained. With a serum dilution of 1 in 250, positive results were as follows: typhus fever—73 out of 73 sera tested, with both *R. prowazeki* and *R. mooseri* antigens; vesicular rickettsiosis—21 out of 22, with *R. conori*, *R. sibiricus* and *R. murinus*; other infections—nil out of 51; healthy persons—nil out of 80. Analysis of results showed that differentiation by the haemagglutination test between epidemic typhus and rat typhus could be achieved in not more than 45% of cases, and that differentiation within the tick-borne spotted fever group was " practically impossible ".

" It thus appears that due to its sensitivity and specificity (provided the result is read from dilutions of 1 : 250) the haemagglutination test can be recommended as a new method of serological group diagnosis for rickettsial diseases belonging to the typhus and tick-borne spotted fever group."

[See also this *Bulletin*, 1953, v. 50, 613 and 1957, v. 54, 1306.]

R. S. F. Hennessey

BIN, Li. **Changes in the Phagocytic Reaction at Various Periods of Immunity during Infection, after Infection and after Inoculation in Experimental Typhus.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 3, 159–63, 3 figs. [12 refs.] [Translated from Russian.]

The phagocytic reaction in guineapigs in experimental infections and prophylactic inoculations is the earliest immune reaction to be detected. A single dose of rickettsial [*R. prowazeki*] vaccine results in a definite phagocytic response but at a lower level than is noted after an experimental infection. A second dose, however, results in an enhanced response in which the infection level is equalled or even passed. The method of recording rickettsial phagocytosis depends on the average number of rickettsiae engulfed per leucocyte; 1–4 rickettsiae are scored as one plus (+), 5–9 as two plus (++) and 10 or more as three plus (+++). Repeated injections of the rickettsial vaccine are necessary for the production of satisfactory agglutinin and complement-fixing antibody levels and also for antibody to neutralize the specific rickettsial toxins.

H. J. Bensted

IABLONSKAIA, V. A. **The Immunogenic Property of the E Strain of *Rickettsia prowazeki*. II. Antitoxic Immunity.** *Problems of Virology.* London. 1959, v. 4, No. 3, 8–10. [Translated from Russian.]

Sera taken from guineapigs 21 days after infection with the E strain of *Rickettsia prowazeki* had much lower antitoxic titres (estimated as the highest serum dilution which, when mixed with 4 LD50 of rickettsial toxin and left at 4–6°C. for 2 hours, protected 50% of mice injected intravenously with the mixtures) than were found in the sera of animals infected with the Breinl strain. Thus, guineapigs infected with a 10^{-3} dilution of a preparation ("dried egg material") of the E strain had an antitoxic titre of 1 in 20 for the homologous toxin and none for Breinl toxin, whereas animals infected with the same dilution of a preparation ("a virulent culture") of the Breinl strain had titres of 1 in 640 and 1 in 1,280 for the E and Breinl toxins respectively. Mice immunized with living rickettsiae of the Breinl strain showed a longer duration of immunity to challenge with rickettsial toxin than did mice immunized with rickettsiae of the E strain. *R. S. F. Hennessey*

KOKORIN, E. N. **Morbid Histology of the Vaccination Process and Morphological Assessment of the Immunity in Guinea-Pigs infected with the E Strains of** *Rickettsia prowazeki*. *Problems of Virology*. London. 1959, v. 4, No. 3, 14–22, 4 figs. [Translated from Russian.]

A study of guineapigs infected intraperitoneally with the E and Breinl strains of *Rickettsia prowazeki* showed that the E strain caused relatively slight signs of peritonitis and insignificant changes in organs other than the brain, where vascular lesions (cellular foci and endothelial proliferation) were sometimes observed. Lesions of this kind occurred in the brains of 15 out of 47 animals inoculated with various dilutions (10^{-1} to 10^{-7}) of an egg preparation of the E strain, whereas they were seen in the brains of 45 out of 47 animals inoculated with the same range of dilutions of the Breinl strain; counts of the lesions indicated that they were some 14 times less numerous in infections with the E strain than in those with the Breinl strain. When the level of immunity present 1½ months after infection was assessed in terms of the frequency with which vascular changes occurred in the brain after challenge with the Breinl strain, it was apparent that infections resulting from an adequate dose (10^{-2}–10^{-3} dilution of dried egg material) of the E strain produced a similar high degree of immunity to that occurring after an infection with the Breinl strain itself; in comparison with the E and Breinl strains, killed typhus vaccine was of low efficacy as an immunizing agent.

On the basis of these histological results, it is concluded that the E strain possesses a very low pathogenicity; as a live vaccine, it is more effective than killed typhus vaccine and can produce a high degree of immunity in guineapigs against infection with the virulent Breinl strain. *R. S. F. Hennessey*

GREIFF, D., POWERS, E. L., KISIELESKI, W. E. & PINKERTON, H. **The Effects of X-Rays and Beta Rays (Tritium) on the Growth of** *Rickettsia mooseri* **and** *Rickettsia akari* **in Embryonate Eggs.** *J. Exper. Med.* 1960, June 1, v. 111, No. 6, 841–9. [15 refs.]

The growth patterns of *Rickettsia mooseri* and *R. akari* in embryonated eggs into which graded doses of tritium oxide were introduced before or after

inoculation showed distinct differences, the growth of *R. mooseri* being accelerated and quantitatively increased by doses in the range of 45 to 180 mc. per egg while that of *R. akari* was markedly inhibited by doses of this order and partially inhibited by doses as low as 11·2 mc. per egg. The growth of *R. akari* was retarded and quantitatively reduced by X-radiation (500 r) of eggs 24 hours after inoculation, but was unaffected by radiation 24 hours before inoculation. (Previous work had shown that the growth of *R. mooseri* was stimulated by X-radiation of eggs [this *Bulletin*, 1957, v. 54, 944].) Direct exposure of *R. mooseri* and *R. akari* to tritium oxide (in a solution with specific activity of 1 c. per ml.) for 6 hours before inoculation into eggs did not affect their growth patterns.

These results indicate that the growth of *R. mooseri*, which usually takes place in the cytoplasm, is accelerated by continuous radiation, while that of *R. akari*, found in both nucleus and cytoplasm, is inhibited. "Since the effects are most probably on the host cells rather than on the organisms, species of organisms such as these selected for their intranuclear or intracytoplasmic growth are valuable test systems for investigations of the relative sensitivities of the nucleus and the cytoplasm, as well as giving information concerning factors governing rickettsial reproduction." *R. S. F. Hennessey*

Le Gac, P. & Giroud, P. L'insuffisance cardiaque aiguë au cours des rickettsioses. **[Acute Cardiac Insufficiency in Rickettsial Infections]** *Bull. Soc. Path. Exot.* 1960, Jan.–Feb., v. 53, No. 1, 20–24, 4 charts. [10 refs.]

This paper is based upon observations made on 6 patients in central tropical Africa, where since 1939 the senior author has described a rickettsiosis which he termed "savannah typhus" [this *Bulletin*, 1940, v. 37, 575; 1946, v. 43, 212, 916 *bis*]. Observations conducted on patients mostly in the district of Oubangui-Chari convinced these authors that cardiovascular episodes of extreme gravity may occur; that they were accompanied in 3 cases by grave psychic manifestations with a tendency to suicide. Detailed case-histories are given for all 6 patients. *Philip Manson-Bahr*

Love, G. J. & Smith, W. W. **Murine Typhus Investigations in Southwestern Georgia.** *Pub. Health Rep.* Wash. 1960, May, v. 75, No. 5, 429–40. 7 figs. [26 refs.]

This paper reports studies of murine typhus in 4 counties of Georgia, U.S.A. Attempts were made to control the disease by applying 10% DDT dust on 5 occasions over 18 months to domestic rat runways and habitats [this *Bulletin*, 1949, v. 46, 347]. The human incidence of infection fell from 174 and 180 per 100,000 to 14·7 and 31·5, while the control area showed no change. Complement-fixation tests on *Rattus rattus* sera for typhus were similarly reduced, and *Xenopsylla cheopis* and *Leptopsylla segnis* were controlled. No reduction was noted in rat mites and lice, and control of *Echidnophaga gallinacea* was erratic. 3 years later [*ibid.*, 1951, v. 48, 976; 1952, v. 49, 34] the incidence had remained low in rats and in man was still dropping, but the vector population was increasing.

Ecological studies of the various components of the host-vector-parasite complex were made. For the interesting findings the paper should be consulted. Eradication of the disease was attempted over a period of 9 months by combining DDT dusting of rat runways with poisoning of commensal rats with anticoagulants [*ibid.*, 1957, v. 54, 1066]. Rats were eliminated from 88% of rural premises but reinfestation occurred steadily and reached a level of 40% in 3 years.

The two forms of control were not strictly comparable; both were effective and each had its advantages. The findings indicated that periodic short-term control operations would probably maintain control indefinitely, and that, since the effectiveness of rat control is proportional to the size of the area freed of rats, operations should cover as large an area as possible. Eradication had advantages over control by dusting in that the reservoir of murine typhus was reduced, public appreciation was greater and savings resulted from rat elimination. These interesting investigations have obvious bearing on plague control.

T. H. Davey

KITAMURA, T. **[Studies on Trombiculid Mites in the Gokase-River District, Miyazaki Prefecture. 3. Isolation Result of *Rickettsia* from Rodents and Successive Survey of Trombiculid Mites]** *Igaku Kenkyo.* Fukuoka. 1960, Apr., v. 30, No. 4, 998–1002, 2 figs. [In Japanese.]

The English summary appended to the paper is as follows:—

"Since the year 1957 the author has been conducting investigation into Trombiculid mites in areas along the basin of the Gokase river of Miyazaki Prefecture and has attempted, in line with the collection of the mites in such localities, to isolate the rickettsia from the spleens and livers of field voles. The number of the surveyed localities was 22, that of isolation attempts was 28 and rickettsia was demonstrated in *Apodemus speciosus* captured in the Totoro Area of Nobeoka City. Although a report has already been made in regard to the mites collected from December, 1957, to April, 1959, 16 *Apodemus speciosus*, 1 *Microtus montebelli* and 3 *Urotrichus talpoides* have been trapped up to the present since the fall of 1959, and 2,335 mites of 8 species have been recovered from these rodents. On the basis of the number of mites collected, *T. kitasatoi* has been predominant in *Apodemus speciosus* and *Microtus montebelli*, followed by *T. fuji* and *G. saduski*, whereas *T. kansai* has been found in large numbers from *Urotrichus talpoides*. However, both *T. daisen* and *T. mitamurai* anticipated at the outset of collection were unable to be collected."

WEYER, F. Experimente mit einem Stamm von Zeckenbissfieber aus Nordqueensland. **[Experiments with a North Queensland Strain of Tick-Bite Fever]** Reprinted from *Schweiz. Ztschr. f. Allgemeine Path. u. Bakt.* 1959, v. 22, No. 5, 609–20, 6 figs. [10 refs.]

The North Queensland strain of tick-bite fever is serologically quite distinct, though it can be cultured in egg yolk like other spotted fever group *Rickettsia*. The author, who has made a study of pathogenic rickettsiae, obtained a culture of *R. australis*, the pathogen of the North Queensland strain, in egg yolk

material. This original material was so concentrated that it was capable of infecting not only guineapigs and mice, but also lice. The guineapigs reacted with fever on the 3rd to 6th days with moderate scrotal reaction and recovered by the 6th day. Mice reacted with pneumonia on the 3rd to 7th days and often died. Mice were inoculated with egg yolk or infected lice. 5 passages over 20 days were made with mouse-lung material, which was full of rickettsiae.

The rickettsiae could also be introduced into mouse peritoneum from egg yolk, mouse lung, infected ticks, lice or mealworms. No clinical signs were observed, but numerous rickettsiae were found in mesothelium cells 5 to 8 days later.

Many infections of lice were successful, by means of rectal inoculation of material from egg yolk, mouse spleen, ticks, mealworms, and the gut, haemolymph or faeces of infected lice. The strain was maintained in lice by 6 passages in 62 days and could have probably continued indefinitely. Natural infection by feeding on infected guineapigs was successful in one test out of 3 (6 out of 10 lice infected). Infection of lice *via* the haemolymph was also successful with repeated passages.

Clearly the louse is a good host for the rickettsiae, which proliferate freely in lice after 5 or 6 days. After rectal inoculation they are found multiplying inside the cells of the gut; the cells, though full, are not distended as with *R. prowazeki* or *R. mooseri*. The lice suffer moderately. In a proportion, the gut becomes permeable to haemoglobin so that the lice turn red and eventually die. Many, however, survived to the end of the test (up to 18 days). Infected faeces are passed.

Rickettsiae inoculated into the haemolymph of lice can be both intra- and extra-cellular. The former attack both functional blood cells and their spindle-shaped precursors.

In other experiments, mealworm larvae (*Tenebrio molitor*) and ticks (*Ornithodoros moubata*) were successfully infected by inoculation into the haemolymph. The rickettsiae remained for considerable periods and could be re-inoculated into mice and lice without loss of their characteristics.

This investigation shows that *R. australis*, like all other forms of *Rickettsia* pathogenic to man, can be maintained in the haemolymph of lice, where it exists (to a large extent) extra-cellularly. Also like all forms (except *R. tsutsugamushi*) it develops in louse gut, multiplies, and appears in the faeces.

The differences between several of these rickettsiae in their relation to lice are apparently matters of degree. *R. australis* is very well adapted to lice and even easier to maintain than *R. prowazeki* and *R. mooseri*. In contrast, some strains of *R. rickettsia* (from Mexico and the Rocky Mountains) can only be maintained for one or two passages in louse gut before they begin to cause severe harm to the lice and fail to develop in the mid-gut cells; they can, however, be maintained by haemolymph inoculation. *R. australis* seems to be most closely allied to South African and Siberian strains of tick-bite fever pathogens.

J. R. Busvine

IGNATOVICH, V. F. **A Contribution to the Question of the Retention of *Rickettsia burneti* on Objects of the External Environment.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 5, 156–7. [Translated from Russian.]

Studies of the survival of *Rickettsia burneti* on various materials on which organisms were allowed to dry and subsequently kept at various temperatures and at a relative humidity of 53–68% showed that the rickettsiae remained viable for periods of between 12 and 16 months on wool stored at 4–6°C., between 7 and 9 months at 15–20°C., and between 1 and 2 months at 34–36°C. On clay and sand, viable rickettsiae were detectable for periods of between 7 and 9 months at 4–6°C., for 4 months at 15–20°C., but not after 2 months at 34–36°C. Rickettsiae on sawdust died more rapidly; they were not found after one month in samples kept between 15 and 36°C. It is thought that the association of rickettsiae with protein when excreted under natural conditions would give considerably greater periods of survival than those mentioned above.

R. S. F. Hennessey

GIROUD, P., LE GAC, P., DUMAS, Nicole & COLAS-BELCOUR, J. Le hérisson *Erinaceus europaeus*, réservoir de rickettsies ou de néo-rickettsies et même d'agents du groupe de l'avortement des ovins. [**The Hedgehog *E. europaeus* as Reservoir of Rickettsiae and Neo-Rickettsiae and Agents of Ovine Abortion**] *Bull. Soc. Path. Exot.* 1959, Nov.–Dec., v. 52, No. 6, 726–30.

In some parts of France, an old saying credits the hedgehog with the ability to cause bovine abortion. An investigation of hedgehogs from areas where the sera of cattle and sheep had given positive results in tests with rickettsial antigens showed that the sera of 4 hedgehogs contained low titres (up to 1 in 20) of agglutinating antibodies for 1 or more of these antigens, including *Rickettsia conori*, *R. prowazeki*, *R. burneti* and the neo-rickettsial strains X14 and Q18 (the last-mentioned being associated with abortion in ewes). Inoculation of mice with material from one hedgehog which had aborted and from another which had died on arrival at the laboratory gave rise to a pneumonic condition, with rickettsia-like bodies in lung smears; similar bodies were seen in preparations from ticks (*Ixodes hexagonus*) taken from a hedgehog.

The authors conclude that there is an epidemiological link between cattle, sheep and hedgehogs, the hedgehogs appearing capable of acting as reservoirs of rickettsiae or rickettsia-like organisms. [This conclusion would seem to need stronger evidence than is presented here.] *R. S. F. Hennessey*

MAGHAMI, G. Séro-agglutination rapide et macroscopique pour la recherche d'anticorps de la Fièvre Q. chez les animaux. [**Rapid Macroscopic Agglutination Method for detecting Q Fever Antibodies in Animals**] *Arch. Inst. d'Hessarek*. Teheran. 1960, June, No. 12, 69–71.

The author, with RAFYI, has already shown the presence of Q fever in animals in Iran, by means of the complement-fixation or agglutination tests [this *Bulletin*, 1955, v. 52, 890]. He now describes a simple slide agglutination test, based on the method used by BRYAN (*Veterinary Medicine*, 1957, v. 52, 111) for rapid agglutination of *Leptospira pomona*. 8 drops of 1% filtered methylene blue in distilled water are added to 5 cc. of antigen (Lederle) of the Nine-Mile strain of *Rickettsia burneti* and left for 2 hours at 6°C. The antigen may be kept at 6–8°C.

For the test, one drop of inactivated serum (56°C. for 30 minutes) is mixed with one drop of the coloured antigen on a slide and stirred with a rod so that a circle of 12–15 mm. diameter is formed. The mixture is examined in good light with the naked eye for 3 minutes, with agitation at the rate of about 25–30 turns a minute. Deep blue agglutination is easily seen in 20 seconds with strongly positive sera and in 3 minutes with weakly positive sera: the clumps gradually accumulate at the periphery of the mixture. Negative sera remain homogenous. 16 positive and 2 negative sera were confirmed by complement fixation; the positive sera gave titres of 1 in 16–1 in 256 and the negative sera remained negative.

The author has used this rapid method successfully with 100 animal sera.

He also compared the test in capillary tubes with that of Luoto who used haematoxylin as the stain [this *Bulletin*, 1954, v. 51, 166]. Positive results appeared in 4 hours at room temperature and in 2 hours at 37°C.: with the author's methylene-blue method, agglutination appeared in 5–15 minutes. Reading should be made within 15 minutes as the agglutinins tend to precipitate thereafter and reading becomes difficult.

The methylene-blue agglutination technique is evidently rapid and requires no special laboratory facilities. *H. J. O'D. Burke-Gaffney*

Berman, S., Cole, G., Lowenthal, J. P. & Gochenour, R. B. **Safety Test for Q Fever Vaccine.** *J. Bacteriology*. 1960, May, v. 79, No. 5, 747–51.

"Embryonated eggs were found to be more sensitive than guinea pigs to small numbers of *Coxiella burnetii* in vaccine and also provided a more reliable system whereby comparatively large volumes of Q fever vaccine could be examined for residual live rickettsiae.

"A method of safety-testing Q fever vaccine in embryonated eggs is described in which no visible rickettsiae in yolk sacs of the 3rd passage eggs was considered satisfactory proof of vaccine safety."

Kordová, N. **Latent Infections in Animals by Filterable Particles of *Coxiella burneti*.** *Acta Virologica*. Prague. 1960, May, v. 4, No. 3, 173–83, 3 figs. (2 on pl.) [23 refs.]

When adult guineapigs, hamsters or mice were inoculated intraperitoneally with filtrates (through membranes of 58 and 40 mμ mean porosity) of suspensions of yolk sacs infected with *Rickettsia burneti*, most of the animals showed no clinical, serological or microscopical signs of infection. Serial passage of splenic material from animals which had shown no response to the inoculation occasionally gave rise to antibody formation in adult animals, but the majority remained "healthy". However, 3-week-old guineapigs inoculated with splenic material from the 5th sub-passage of filtrate in adult guineapigs developed typical infections with *R. burneti* after an incubation period of 9 to 14 days. Typical *R. burneti* were also isolated in egg and tissue cultures of splenic material from apparently uninfected guineapigs, hamsters, mice and chicks

which had been inoculated with filtrates or passaged filtrate material (in the case of chicks, the isolations were made from pooled liver, spleen and lung tissue).

The author considers that these results point to the passage of specific genetic material of *R. burneti* through the filters, this material being capable of persisting in a latent form in apparently healthy animals and of developing into typical "mature" rickettsiae under suitable conditions. He assumes that the filterable particles represent an intracellular stage of the developmental cycle of *R. burneti*, a stage which may correspond to the vegetative genome postulated by LWOFF as occurring in latent viral infections.

R. S. F. Hennessey

SOMOVA, A. G.; SILICH, V. A.; POLIAKOV, I. I.; KHAKHINA, Z. D.; GERASIUK, L. G. **Experimental Mixed Q Fever and Brucellosis Infection. I. Peculiarities of the Course of Q Fever** [SOMOVA, SILICH, POLIAKOV, KHAKHINA & GERASIUK]. *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 3, 126–33, 2 figs. **II. Features characterizing the Course of Brucellosis** [POLIAKOV, SOMOVA, SILICH, KHAKHINA & GERASIUK]. *Ibid.*, 133–8, 2 figs. [Translated from Russian.]

I. Guineapigs infected with *Rickettsia burneti* 30 days after infection with *Brucella melitensis* showed a higher temperature, a longer febrile period, and higher complement-fixation titres for *R. burneti* antigen, than did animals which received *R. burneti* alone, *R. burneti* and *B. melitensis* simultaneously, or *R. burneti* 15 days after infection with *B. melitensis*. In passage experiments to determine the persistence of *R. burneti* in organs (pooled spleen, liver and kidney) of guineapigs infected in these various ways, 10 out of 10 animals infected with *R. burneti* 30 days after infection with *B. melitensis* were apparently free of the rickettsial infection 30 days later, whereas 3 out of 10 animals which received *R. burneti* 15 days after infection with *B. melitensis* were carrying transmissible rickettsiae 30 days later. Serological cross tests showed no antigenic relationship between *R. burneti* and *B. melitensis*.

II. Bacteriological studies of tissues from guineapigs infected with *R. burneti* and *B. abortus* simultaneously or in that order showed that dissemination of *B. abortus* was less marked than in animals infected with *B. abortus* only. Agglutinin titres for *B. abortus* were significantly higher in the sera of animals infected with this organism only than in those of animals with mixed infections. The development of allergic reactivity towards brucellin, and of increased phagocytic activity towards *B. abortus*, was not affected by previous or concurrent infection with *R. burneti*. Animals infected first with *B. abortus* and later with *R. burneti* showed no significant difference in the degree of dissemination of *B. abortus* when compared with animals infected with *B. abortus* alone.

R. S. F. Hennessey

YELLOW FEVER

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control.

Briceño Rossi, A. L., in collaboration with R. Isaac Diaz & Helena Segura Nota previa al estudio de los virus Arbor en Venezuela. [**Preliminary Note on the Study of Arborviruses in Venezuela**] *Gac. Méd. de Caracas.* 1960, Jan.–Mar., v. 68, Nos. 1/3, 45–50.

This paper, from the virus section of the National Institute of Hygiene (Yellow Fever and Plague Division) in Caracas, records the isolation of a virus from a sylvan monkey *Alouata seniculus seniculus*, captured in Los Claveles, Cojedes State, Venezuela, where a fatal epizootic disease in monkeys had been reported. Full details are given of laboratory studies: the virus showed the characters of yellow-fever virus in protection tests and in histopathological examination of the liver. This is stated to be the first isolation of yellow-fever virus from sylvan monkeys in Venezuela. *H. J. O'D Burke-Gaffney*

Panthier, R. & Hannoun, C. Virulence pour l'embryon de poulet du virus vaccin amaril. [**Virulence of Yellow Fever Vaccine for Chick Embryos**] *Bull. Soc. Path. Exot.* 1960, Jan.–Feb., v. 53, No. 1, 100–105.

A 17D yellow-fever vaccine which had not been lyophilized, and Dakar vaccine, were inoculated in the neighbourhood of the embryo in 7-day chick embryos. With a dose of 8,000 mouse intracerebral LD50 of Dakar virus 9% of 56 embryos died from 6 to 12 days after inoculation but only 9% of the chickens hatched. With a similar dose of 17D virus 94% of 63 embryos died 3 to 12 days after inoculation, most of them 5 days after inoculation; none of the remainder hatched. With 8 LD50 of 17D 49% had died by 12 days after inoculation, 61% with 80 LD50 and 86% with 800 LD50. 90% of control embryos which had been submitted to the inoculation procedure without virus hatched.

When hyperimmune horse serum was mixed with 85 LD50 of virus [? strain] 9 of 10 embryos inoculated hatched; with serum plus 850 LD50, 8 of 10 hatched.

In a comparison of eggs incubated at 36°C. and 39°C., the mortality was similar, but lesions were more severe at 39°C.: there was oedema of the chorio-allantoic membrane. Lyophilized virus was found to give more irregular results. *C. E. Gordon Smith*

RABIES

Kaplan, M. M., Wecker, E., Forsek, Z. & Koprowski, H. **An Indicator Plaque-Forming System for Demonstration of Interference by Non-Cytocidal Strains of Rabies Virus.** [Correspondence.] *Nature.* 1960, June 4, v. 186, 821–2.

Although strains of fixed rabies virus multiply in chick embryo tissue cultures they do not cause cytopathic changes; they do, however, interfere with cytopathic viruses.

Chick embryo monolayers were exposed for 2 hours to $10^{6.2}$ mouse LD50 of a fixed strain (CVS) of virus. Fluid medium was then added and the monolayers were incubated for 24 hours. The cells were then exposed to western equine encephalitis virus for 45 minutes, after which they were overlaid with agar, incubated, and subsequently stained to reveal plaque formation. Up to 2 million plaque-forming units of western equine virus were inhibited. One inhibiting unit of rabies virus was about $10^{3.5}$ mouse LD50. Results were reproducible and the effect was neutralized by specific rabies antiserum. Street virus seems to behave similarly.

Interferon was prepared by centrifugation and serum neutralization of the culture fluid after 24 hours' growth of rabies virus in monolayers. This interfered with 10–1,000 plaque-forming units of western equine virus.

Neutralizing antibody could be estimated in the same way by plating mixtures of rabies virus and dilutions of the antiserum after incubation.

C. E. Gordon Smith

Schindler, R. Untersuchungen über die Bedeutung eines bei Karnivoren vorkommenden Speichelfaktors mit Hyaluronidase-ähnlicher Wirkung für die Übertragung der Tollwutinfektion. Teil I. [**Investigations on the Significance of a Saliva Factor with Hyaluronidase Activity in Carnivores in the Transmission of Rabies Infection. Part I.**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1959, Dec., v. 10, No. 4, 450–76.

The addition of hyaluronidase to the infective inoculum caused a slight increase in mortality in mice infected intramuscularly with the Pitman-Moore strain of rabies virus, but no effect was noted on intracerebral infection. The rate of disappearance of the virus from the site of intramuscular injection was accelerated by the addition of hyaluronidase. The results are discussed in relation to the pathogenesis of rabies.

D. J. Bauer

Constantinescu, N., Cajal, N., Bîrzu, N., Cepleanu, M. & Zavate, O. Infecția rabica experimentală la hamsterul sirian. [**Experimental Rabies Infection in the Syrian Hamster**] *Studii si Cercetări Inframicrobiol.* 1960, v. 11, No. 1, 61–72, 5 figs. (1 on pl.) [29 refs.] French summary.

A study has been made of the susceptibility of hamsters to infection with rabies virus. After intracerebral injection with 3 strains of street virus paralysis developed after 7–19 days and sometimes lasted for up to 20 days before death

supervened. A stage of excitation was not observed. In parallel titrations of an infected human brain hamsters gave essentially the same titre as mice and rats. In hamsters infected with the Babes strain of fixed virus the incubation period was 4–5 days after intracerebral and 6–9 days after intramuscular injection, and the virus could be found in the brain in titres up to 10^{12} [*sic*]. Negri bodies were found in large numbers in hamsters infected with street virus, and similar inclusions were also found after infection with fixed virus. *D. J. Bauer*

PISKAREVA, N. A., PISAREVA, N. A. & IVANOV, N. P. **Development of a Method for the Inactivation of Rabies Vaccine with Ultra-Violet Radiation. I. The Influence of Different Conditions of Ultra-Violet Irradiation on the Ineffectivity and Immunological Properties of Fixed Rabies Virus.** *Problems of Virology*. London. 1959, v. 4, No. 4, 34–8, 1 fig. [Translated from Russian.]

The vaccine was made from rabbit brain infected with the Leningrad strain of fixed rabies virus. A 5% brain suspension in 10% sucrose buffered at *p*H 7·2–7·4 was irradiated with ultra-violet light in a film <0·01 mm. in thickness in an apparatus described. Vaccine was tested for live virus by intracerebral inoculation of mice with 2–3 blind passages where necessary. The minimal conditions for inactivation by this criterion were a flow of 3,600 ml. per hour with the U-V lamp 100 mm. from the surface of the fluid. Vaccine potency was estimated in a Habel test and by testing the pooled sera of immunized mice for neutralizing antibody. After inactivation in the above conditions, material with an initial infectivity of 7·0 log LD50 yielded a vaccine which gave a resistance index of 5·0 log and mouse sera with a neutralizing index of 6·0 log. *C. E. Gordon Smith*

GREENBERG, M. & CHILDRESS, Jean. **Vaccination against Rabies with Duck-Embryo and Semple Vaccines.** *J. Amer. Med. Ass.* 1960, May 28, v. 173, No. 4, 333–7, 1 fig. [18 refs.]

Between July 1957 and May 1959 the authors compared the antibody titres and the general and local reactions produced in patients given injections of duck-embryo vaccine and Semple-type brain tissue vaccine, respectively, at the antirabies clinics of the New York City Department of Health. To enable such comparison to be made, one group of patients received 0·5 ml. daily of Semple-type vaccine (20% suspension) and the other 1·0 ml. daily of duck-embryo vaccine (FVS strain of rabies fixed virus, single passage in duck-embryo and inactivated with 1 in 4,000 beta-propiolactone), the vaccines being administered subcutaneously on 14 consecutive days. From as many as possible of those vaccinated (about 120 in each group) blood specimens were obtained before the first injection and thereafter between the 7th and 10th day, the 11th and 15th day, the 31st and 60th day and the 6th and 9th month. In the serum-virus neutralization tests for antibody titration doubling dilutions of serum were mixed with equal quantities of a constant dilution of the CVS rabbit-fixed strain of rabies virus (100 LD50 per mouse inoculum). 6 mice were used for each serum dilution and, after intracerebral inoculation each with 0·03 ml. of

the serum-virus mixtures, were kept under observation for 14 days. 50% end-points were calculated by the Reed and Muench method.

Results of these tests on the 2 groups of treated persons, in none of whose pre-vaccination serum samples had rabies antibodies been demonstrable, showed that by the 10th day after the commencement of vaccination all but 22 (26·5%) of the 83 receiving duck-embryo vaccine had antibody titres in the range of 1 in 4 or higher, while 51 (64·6%) of the 79 receiving Semple vaccine had no neutralizing antibodies. By the 15th day all but about 15% of both groups had measurable antibodies, with titres in the range of from 1 in 4 to 1 in 128. Between 1 and 2 months after the first injection of either vaccine the rate of immunization was 93% for those who received duck-embryo vaccine and 97% for those who received Semple vaccine. By 6 to 9 months after the first injection measurable antibodies had dropped to about 88% in both groups. As regards complications of treatment: local reactions were about the same in both groups, but among those treated with Semple vaccine there were 2 cases of encephalomyelitis.

Restimulation of the immunity induced by previous antirabies vaccination was then investigated. 63 persons, who returned about 7 months after the primary series of injections, were given a booster dose of the vaccine they had originally received; all responded satisfactorily, the antibody titres evoked by both types of vaccine being, in general, much higher than after the primary series of injections. Of 6 persons who at the time of their reporting at the clinics had histories of treatment 2–17 years previously with Semple vaccine and whose pre-inoculation sera were found still to have antibody titres of 1 in 4 to 1 in 41, 4 received a full course of duck-embryo vaccine and 2 one of Semple vaccine; in all these persons a marked booster effect was obtained, irrespective of the type of vaccine used. Again, of 6 veterinarians who had received injections of Semple vaccine in the past and who were given a single dose of duck-embryo or Semple vaccine, all responded with a booster type of increase in titre, even the 2 without measurable antibody titre before they were given the booster dose. One veterinarian, for example, who had received only 3–4 injections of Semple vaccine 19 years previously and who had a serum titre of zero before the booster dose was given, achieved a titre of 1 in 555 after the booster. Booster effects, therefore, were readily obtained with both vaccines.

In the authors' view " the earlier development of antibodies and the absence of the complication of encephalomyelitis after the use of duck-embryo vaccine suggests its use in the prophylaxis of rabies in preference to vaccines containing brain tissue ". *G. Stuart*

BRIGGS, G. W. & BROWN, W. M. **Neurological Complications of Antirabies Vaccine. Treatment with Corticosteroids.** *J. Amer. Med. Ass.* 1960, June 18, v. 173, No. 7, 802–4. [11 refs.]

" A patient with rapidly ascending encephalomyelitis after 12 injections of Semple-type antirabies vaccine (rabbit central nervous system preparation) apparently responded dramatically to the administration of corticosteroids."

[See this *Bulletin*, 1954, v. 51, 169].

BURNS, K. F., SHELTON, Dorothy F., LUKEMAN, J. M. & GROGAN, E. W. **Cortisone and ACTH Impairment of Response to Rabies Vaccine.** *Pub. Health Rep.* Wash. 1960, May, v. 75, No. 5, 441–5, 1 fig. [12 refs.]

In controlling the various allergic and paralytic reactions which complicate antirabies treatment with nervous tissue vaccines the value of cortisone and of corticotrophin has frequently been reported. In the present article the authors show the effect of such corticosteroids on the neutralizing antibody response to antirabies vaccination. This effect was first studied in a male patient with the following case history. Immediately after exposure he was given 11,000 units of antirabies serum and then 0·5 ml. of Harris-type vaccine was administered daily on 14 consecutive days. On the 7th day of treatment urticarial and anaphylactoid reactions developed and, in consequence, steroid therapy was instituted, *viz.*: oral cortisone from the 7th to the 24th day in a total dosage of 4,200 mgm.; intravenously administered hydrocortisone, 100 mgm. on the 7th and again on the 9th day; and intramuscular corticotrophin gel (a mixture of corticotrophin in gelatin) in daily dosages of 80 units from the 9th to the 16th day and of 40 units from the 17th to the 25th day. By the 27th day reaction symptoms had disappeared.

Serological examination of the patient's blood revealed a high level of neutralizing antibody for 21 days, but thereafter the titre fell rapidly, no evidence of active immunity being detectable after the 24th day. The obvious failure of the vaccine to immunize might well have been due to the concomitant administration of steroids, and in order to investigate this possibility animal experiments were undertaken.

30 fully grown rabbits were divided into 5 groups of 6 each. Therapy was administered to each group as follows: to group 1, rabies vaccine alone; to group 2, rabies vaccine and cortisone; to group 3, rabies vaccine and corticotrophin; to group 4, cortisone alone; and to group 5, corticotrophin alone. Groups 1, 2 and 3 received subcutaneously 14 daily doses, each of 0·5 ml., of a 1 in 10 dilution of Harris-type vaccine (a living attenuated virus prepared by suspending in sterile distilled water the brains of rabbits infected with attenuated fixed rabies virus). Group 2 received, in addition to the vaccine, cortisone acetate in 14 daily doses of 5 mgm. each by intramuscular injection. Group 3 received, in addition to the vaccine, corticotrophin intramuscularly in 14 daily doses, each of 20 international units (IU). Groups 4 and 5 received, respectively, cortisone alone and corticotrophin alone, in identical dosage and by the same route as Groups 2 and 3. All animals in each group were bled prior to inoculation and 15, 30 and 53 days after initiation of therapy. The neutralizing capacity of each serum was expressed as the log neutralization index (NI), *i.e.*, the difference in log LD50 end-points of a given serum-virus mixture as compared with the appropriate pre-inoculation serum. A serum was regarded as positive if the NI was 1·7 or greater, as negative if the NI was less than 1·0 and as equivocal if the NI was between 1·0 and 1·7. Rabies standard challenge virus (CVS) was employed as the test virus.

Results of neutralization tests performed on the 53rd post-inoculation day showed that in group 1 all 6 rabbits had positive NI's of 2·0 to 3·8; that in group 2, of the 5 animals which survived, 4, with NI's of from 0·0 to 0·8, had no significant immunity, while 1 had an equivocal NI of 1·5; that in group 3, of the 5 surviving rabbits, 4 with NI's of 2·0 to 2·9 yielded positive antibody

responses, while 1 had an equivocal NI of 1·5; and that in groups 4 and 5, as well as in untreated control animals, there was no change in immunological status.

These results indicate that cortisone interferes with the active immunity ordinarily conferred by antirabies vaccine and that corticotrophin, although slightly depressing their titres, does not prevent the formation of neutralizing antibodies. For allergic reactions occurring during the administration of antirabies vaccine and requiring control by steroid therapy it would appear, therefore, that corticotrophin is the drug of choice and that cortisone is contraindicated. Finally, it has to be observed that, as shown in the single human case studied, neither cortisone nor corticotrophin affects adversely the passive immunity conferred by the injection of antirabies serum. *G. Stuart*

i. Mirchamsy, H., Razavi, J. & Bahmanyar, M. **Preparation of Antirabies Serum from the Mule.** *Arch. Inst. d'Hessarek.* Teheran. 1960, June, No. 12, 73–9.

ii. ——, Korour, A. & Bahmanyar, M. **Electrophoretic Study of Antirabies Serum. Practical Application.** *Ibid.*, 81–4, 2 figs.

iii. ——, Nazari, F. & Bahmanyar, M. **Concentration of Antirabies Serum.** *Ibid.*, 85–9, 4 figs.

These 3 papers relate to the hyperimmune antirabies serum produced at the Razi Institute, Iran.

i. In the first paper details are given of the technique employed for preparing in mules a powerful mixed antirabies and antitetanus serum at the same time by simultaneous injections of the corresponding antigens. For this double immunization use was made of the following antigens: for the preparation of antirabies serum—freshly prepared 5% suspensions of sheep brain infected with Sassari virus, phenolized (0·5%) and inactivated for 24–48 hours at 37°C., as well as non-phenolized and non-inactivated; and for the preparation of antitetanus serum—purified tetanus toxoid absorbed on aluminium phosphate (PATT). The basic immunization schedule involved the use of the Fermi-type vaccine in doses increasing from 20 to 45 ml. daily over a period of 56 days, during which 25 and 40 ml. of PATT were administered on the 21st and 41st days, respectively. After a 60-day interval a second series of inoculations was begun on the 117th day and continued to the 143rd day, during which period Fermi-type vaccine was given in doses of 30 to 45 ml. on the first 20 days, live virus suspension in a daily dosage of 30 ml. on the remaining 16 days, and PATT in doses of 30, 45 and 60 ml. on the 117th, 127th and 137th days, respectively.

Serum-virus neutralization tests in mice on a first harvest bleeding of 8 mules and 7 horses so treated showed that all 8 mules had responded to this basic immunization, with a rabicidal antibody titre superior to that in the 5 horses which responded. 2 hyperimmunizing series of inoculations were then carried out: the first, on both mules and horses, between the 243rd and 266th days, with 25 to 35 ml. of Fermi-type vaccine daily and 25 ml. of PATT on the 243rd day; the second, only on mules, begun 100 days later and effected over a

like period and with the same dosage as the first. The results of serum-neutralization tests on animals bled 12 days after completion of the first hyperimmunizing series showed a spectacular difference between the rabicidal antibody titres of mules and horses; in mules the titres, expressed in international units per ml., reached levels between 140 and 320, whereas in horses the level showed little change from that (40) resulting from basic immunization. After the second hyperimmunizing series the titres in the mule sera reached levels above 320 to a maximum of 800, as compared with a titre of 87 units per ml. in the international reference serum. As regards the response given by the test animals to PATT, the number of international units per ml. varied between 200 and 330 in the mule sera and between 45 and 110 in the horse sera.

As, in the authors' experience, the mule is not refractory to immunization, it is held to be the animal of choice for the preparation of antirabies serum.

ii. In the second paper, which stresses the need for early and repeated evaluation of antibody response in animals used for the production of hyperimmune antirabies serum, the authors describe a method whereby the antirabies fraction in immunized animals' sera may be ascertained and the precise dilutions of such sera for titration in mice by the serum-virus neutralization test determined. By application of this method—that of paper electrophoresis—it was demonstrated that during hyperimmunization there developed a fraction normally slight or absent in mules. This fraction, found between the beta 1 and gamma globulins and known as fraction T or beta 2 globulin, increased during immunization until it represented 17–25% of the serum fractions in the hyperimmunized mule. Concurrently a marked decrease of albumin was noted, as well as a slow and very slight decline in the gamma globulin fraction. Further investigation showed a constant relationship to exist between the increase in beta 2 globulin and the increase in rabies antibody.

For the accurate titration of rabies antibody the electrophoretic method is not claimed to be a substitute for the serum-virus neutralization test in mice, but by indicating the serum dilutions to be used in that test it effects a considerable economy in the number of mice ordinarily required for the determination of serum antibody titre.

iii. In the third paper the authors compare the results obtained with 3 methods used for the concentration of antirabies serum, *viz.*, 2 enzymatic digestion procedures and the ammonium sulphate fractionation method. These results showed the enzymatic digestion procedures to give products of the same order as regards concentration, but with a very much lower yield (5·6 to 22%) than that (40 to 62%) given by the ammonium sulphate method. As, under working conditions at the Razi Institute, the ammonium sulphate concentration method, with decolorization by means of aluminium hydroxide, has been found to give a product with a 3–6 times higher concentration of neutralizing antibody than the crude serum, the authors consider it to be the method of choice. *G. Stuart*

Nicolau, S. S., Constantinescu, N., Bîrzu, N. & Zavate, O. Imunitatea în turbare apreciată prin testul peritoneal de neutralizare a virusului rabic. **[Immunity in Rabies Determined by the Intraperitoneal Neutralization Test with Rabies Virus]** *Studii si Cercetări Inframicrobiol.* 1960, v. 11, No. 1, 9–19. [16 refs.] French summary.

The authors have developed a peritoneal neutralization test for the determination of immunity in animals treated with Fermi-type rabies vaccine, in which a suitable dilution of a brain suspension infected with the Babes strain of fixed rabies virus is injected intraperitoneally, withdrawn after 60–90 minutes and then injected into mice intracerebrally. Survival of the mice is regarded as evidence of the presence of immunity. The method was used to demonstrate immunity in hamsters, mice and rats which had received Fermi vaccine up to 163 days previously, and neutralization was also obtained with animals which had developed rabies after the intraperitoneal injection of live fixed or street virus. *D. J. Bauer*

HUYGELEN, C. **Antirabic Immunity in Guinea-Pigs induced by High Egg Passage Flury Virus. The Influence of the Route of Administration on the Resistance to Cerebral and Extraneural Challenge.** *J. Hygiene.* 1960, June, v. 58, No. 2, 187–91. [29 refs.]

In the experiments reported in this paper the author compares the degree of immunity in guineapigs vaccinated intracerebrally with that in other guineapigs vaccinated peripherally. In both instances some animals received the challenge inoculation by the intracerebral route and others received it peripherally. The Flury strain used in the experiments was at its 195th egg passage (HEP) and was no longer pathogenic for adult mice on intracerebral inoculation; it had also almost completely lost its pathogenicity for guineapigs when introduced intracerebrally in high concentrations. Before use the virus was titrated in 4-day-old baby mice and showed a titre of $10^{-3.5}$. The CVS strain of rabies fixed virus, with a titre of $10^{-6.5}$ in adult mice, was employed for challenge purposes. In the immunization experiments guineapigs of 350–400 gm. weight were used. For intravenous inoculation only male guineapigs were employed and the injection was given into the veins of the penis.

In the first experiment 3 groups of guineapigs received each 0·2 ml. of a 1 in 10 suspension of the HEP Flury virus. In group A (25 animals) the virus was introduced intracerebrally, in group B (30 animals) intravenously and in group C (30 animals) intramuscularly (in the gastrocnemius muscles). 21 days after administration of the Flury strain all guineapigs in the 3 groups and all 30 control animals were challenged intracerebrally with 0·2 ml. of serial ten-fold dilutions of CVS, ranging from 10^{-2} to 10^{-6} in group A and from 10^{-2} to 10^{-7} in groups B and C and in the control group. 5 guineapigs were used for each dilution and all were kept under observation for 21 days. Results showed the LD50 (calculated by the method of Reed and Muench) to have reached $10^{-5.7}$ in the control group, $10^{-5.3}$ in group B and $10^{-4.3}$ in group C. From these results it is apparent that the log of protection afforded by the vaccine—found by subtracting the log of 50% end-point in the vaccinated animals from the log of 50% end-point in the controls—was only 0·4 in group B and 1·4 in group C [as compared with the log 3 required to meet minimum standards]. In group A the LD50 could not be determined, as only 1 animal in the whole group succumbed to the challenge inoculation.

In the second experiment 2 groups of 40 guineapigs were immunized with the same dosage as that used in the first experiment. The first group was inoculated intracerebrally and the second group intramuscularly. 21 days later all

guineapigs in the 2 test groups and 40 control animals were challenged by injections of 0·5 ml. of serial two-fold dilutions of CVS (1 in 20–1 in 1,280) into the masseter muscles. Results showed a high mortality rate in the control group and a very high degree of immunity in both vaccinated groups: thus, for example, when challenged with 1 in 20 to 1 in 160 dilutions of CVS, 21 of 22 control animals died of rabies, while only 1 of 23 animals vaccinated intramuscularly and none of 24 vaccinated intracerebrally succumbed to identical challenge inoculations.

The combined results of the above immunization experiments in guineapigs with HEP Flury virus permit the following conclusions to be drawn: intracerebral inoculation of the vaccine protects against later intracerebral or peripheral challenge with rabies fixed virus; intramuscular administration of the vaccine results in the development of satisfactory resistance to peripheral challenge; and intramuscular or intravenous inoculation of the vaccine fails to protect against intracerebral challenge. *G. Stuart*

PLAGUE

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, rodent hosts, transmission, pathology, diagnosis, clinical findings, treatment, control.

MEAD, Dorothy D., WESSMAN, G. E., HIGUCHI, K. & SURGALLA, M. J. **Stability of Cell Suspensions of *Pasteurella pestis* at 5 C and at −23 C.** *Applied Microbiol.* Baltimore. 1960, Jan., v. 8, No. 1, 55–60. [14 refs.]

Suspensions of *Pasteurella pestis* containing more than 10^{10} bacterial cells per ml. can be stored in the frozen state for long periods of time with little loss of virulence or viability. Survival at temperatures above freezing is, however, severely affected by certain environmental conditions: the availability of oxygen, concentration of the bacterial cells in the suspension, the *p*H of the suspending medium and the nutritional conditions under which the organism was grown. Storage at +5°C. under optimal conditions of surface-to-volume ratio, with high buffering and cell concentrations in the region of 1×10^{10}/ml. resulted in a 50–75% viability over a period of 12 weeks, but loss of virulence began to appear after 4 weeks and there was a definite shift towards avirulence between the 4th and 8th weeks. At 12 weeks there was evidence of a greatly reduced virulence but partial recovery could be effected by making subcultures and incubating the freshly inoculated slants at 26°C. The mechanism involved in the loss of virulence at +5°C. is not understood but it would seem to be more than a population change. Cells grown at 5–10°C. are relatively avirulent but virulence is regained with a short incubation at 37°C. and as suspensions held at +5°C. actively metabolize it seems likely that physiological change plays a predominant role in this loss of virulence. *H. J. Bensted*

BROWNLOW, W. J. & WESSMAN, G. E. **Nutrition of *Pasteurella pestis* in Chemically Defined Media at Temperatures of 36 to 38 C.** *J. Bacteriology*. 1960, Feb., v. 79, No. 2, 299–304, 1 fig. [11 refs.]

The nutritional requirements of *Pasteurella pestis* were studied at temperatures 36–38°C. because it had previously been shown that these requirements are much more exacting as the temperature approaches the range of body temperatures of warm-blooded animals susceptible to plague. A chemically defined medium that proved satisfactory for optimal growth at 28°C. was found to be inadequate at higher temperatures. Some amino acids were essential for all the strains tested, but some strains were more fastidious, and as the temperature increased from 36° to 38°C. further additions became necessary.

H. J. Bensted

SMITH, J. L. & HIGUCHI, K. **Studies on the Nutrition and Physiology of *Pasteurella pestis*. V. Inhibition of Growth by D-Serine and its Reversal by Various Compounds.** *J. Bacteriology*. 1960, Apr., v. 79, No. 4, 539–43, 2 figs. [17 refs.]

The inhibitory effect of D-serine on the growth of a number of different types is well known. GLADSTONE demonstrated the effect of D-serine on the growth of anthrax bacilli in 1939 (*Brit. J. Exper. Path.*, 1939, v. 20, 189) and several other groups of workers have reported similarly with regard to its inhibitory effect on growth, depression of toxin formation, and suppression of spore formation. The present authors have already reported on the sensitivity of *Pasteurella pestis* to D-serine [this *Bulletin*, 1958, v. 55, 1006] and they show in this paper that almost complete inhibition of the growth of *P. pestis* resulted from the presence of D-serine in a concentration of about 1 mM. No inhibitory effect was obtained with L-serine, even in concentrations as high as 25 mM. Several amino acids were capable of reversing the effect of D-serine; glycine, however, was particularly effective in this respect, much more so that L-alanine. Xanthine and adenosine were capable of only partial reversal and other purines or purine derivatives were without effect. It is suggested that D-serine inhibits growth of *P. pestis* by blocking entry of glycine into purines and other compounds.

H. J. Bensted

LAWTON, W. D., FUKUI, G. M. & SURGALLA, M. J. **Studies on the Antigens of *Pasteurella pestis* and *Pasteurella pseudotuberculosis*.** *J. Immunology*. 1960, May, v. 84, No. 5, 475–9. [20 refs.]

Representative cultures of the two organisms, virulent and avirulent in each case, were examined by an agar gel diffusion technique and 18 antigens were identified, 5 of which were specific for *Pasteurella pestis* and 2 were specific for *P. pseudotuberculosis* and 11 were common to both.

Equal size batches of guineapigs were immunized with 4 different vaccines, (a) a commercial anti-plague vaccine; (b) an anti-fraction-1 vaccine; (c) an attenuated live vaccine (EV 76); and (d) a killed *P. pseudotuberculosis* vaccine. Vaccines (a), (b) and (c) induced protection against challenge with virulent plague bacilli and also against *P. pestis* Fraction 1, but no protection against

this factor was obtained with vaccine (d). L-antigen, which was found to be present in all the cultures examined, was represented in the sera obtained from the guineapigs inoculated with the live vaccine and the killed vaccine prepared from *P. pseudotuberculosis*, but the purified L-antigen offered no protection against *P. pestis* infections.

When the sera from the immunized animals were analysed they showed a promising correlation between specific circulating antibodies, anti-L-factors and immunity to pneumonic plague. *H. J. Bensted*

MUNSHI, D. M. **Micro-Anatomy of the Proventriculus of the Common Rat Flea *Xenopsylla cheopis* (Rothschild).** *J. Parasitology*. 1960, June, v. 46, No. 3, 362–72, 9 figs. on 3 pls. [27 refs.]

KOTLIAROVA, R. I. **A Study of the Part played by Separate Fractions of Plague Immune Sera in the Prevention and Treatment of Plague.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 3, 152–8, 2 figs. [Translated from Russian.]

Gamma globulin, beta globulin and alpha globulin fractions prepared from an antiplague serum (which does not appear, itself, to have been standardized in any way) were compared in relation to their prophylactic and therapeutic properties with the original raw preparation against a low and a high level challenge in mice. The various immune preparations were injected 24 hours before, simultaneously with, and 24 and 48 hours after the challenge. Even with low level challenge the raw serum appeared to have low protective values but the gamma globulin fraction gave about 70% protection when injected before or at the time of challenge at the low level; at high level challenge the protection was considerably less. The beta globulin showed some protection but significantly less than the gamma globulin fraction. The alpha globulin fraction appeared to be immunologically inactive. No information is given about the strains used for the preparation of the antiplague serum, the method used, or the exact nature of the challenge except that low challenge was just sub-lethal and high challenge 4 times this dose. No references are given other than those of workers within U.S.S.R. *H. J. Bensted*

CHOLERA

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

SEATO Cholera Research Project. Thailand [LUANG BINBAKYA BIDYABHED, Director General]. Quarterly Report. 1 Dec. 59 to 29 Feb. 60. 9 mimeographed pp. 1960. Bangkok.

As a result of the cholera epidemic in Thailand early in 1959 a cholera research laboratory was established in the Royal Thai Army Institute of

Pathology in Bangkok with the help of the U.S. Army Cholera Research Team and a section of the U.S. Naval Medical Research Unit Two (NAMRU 2). The successful cooperation between the United States and Thai workers in dealing with the epidemic showed what could be done by the combined investigations of trained teams of research workers, and it was decided that a comprehensive programme should be developed for the more intensive study of the disease which it was hoped would result in better methods of prevention and control.

The projected scheme as detailed in this report depends on the continued help from the United States with personnel for at least the early period of the existence of the Thai SEATO cholera laboratory. Certain other help would also come from the same source. Technical training of Thai personnel has been the first need and improved facilities for training both bacteriologists and epidemiologists have been fully considered in the project.

The research projects themselves fall under three main headings, each of which has a Project Director: (a) Physiological Studies—water and electrolyte metabolism, production of diarrhoea, *p*H etc.; (b) Epidemiological Studies—this would cover all diarrhoeal diseases; (c) Bacteriology—this includes improved diagnostic methods, intensive study of the vibrios, immunity reactions, cholera toxins, phage etc.

There are few aspects of cholera research that have been overlooked and the programme is an ambitious one. It would appear, however, that although the organizers are anxious to commence these investigations as soon as possible it will not be feasible to develop the project successfully without further help. This report is intended, in part at any rate, to interest other SEATO nations in the project and to attract workers and finance from these countries for its support. *H. J. Bensted*

SEAL, S. C. **The Problem of Cholera in India.** *Indian J. Pub. Health.* 1960, Jan., v. 4, No. 1, Suppl., 1–27, 5 charts (1 folding), 1 graph & 5 maps. [34 refs.]

The author, who is Professor of Epidemiology at the All India Institute of Hygiene and Public Health, Calcutta, gives a general account of the history and distribution of cholera, with special reference to the Indian sub-continent. The distinguishing features of endemic areas in India are:

(1) cases are more concentrated in the deltaic tracts than elsewhere;
(2) they are generally within 100 miles of the sea-coast;
(3) the water sources in such areas have a high salinity and sometimes higher *p*H;
(4) the population in such areas is invariably rice-eating and has generally a high density;
(5) the temperature and humidity are generally high.

Movement of population is an important factor in the production of epidemics, and wherever this is a constant factor the disease persists permanently in the area, *e.g.* in Calcutta and its surrounding industrial belt. Other contributory factors are social and economic conditions and the state of environmental sanitation. The handling of an epidemic situation is much easier and simpler than that of an endemic situation.

The commonest and most potent social factor in the perpetuation of cholera in India is the aggregation of population, often in huge numbers, in connexion with fairs and festivals, which are held at almost every period of the year in one place or another. The most important pilgrim centres serve as a constant source for the spread of infection. Famine, floods and earthquakes have often been followed by a rise in the incidence of cholera, but the more constant social factors favouring the spread of the disease are poverty, ignorance and insanitary health habits. Thus in Calcutta cholera occurs chiefly among the poor and illiterate, and largely among the population living in the slum areas known as *bustees* [this *Bulletin*, 1959, v. 56, 298; 1960, v. 57, 32].

Data are presented relating to the seasonal prevalence of cholera in the various Indian States and tables are included showing mortality figures by quinquennial periods from 1877 to 1956 and annual mortality rates in the different States from 1939 to 1958. These features are also illustrated in a number of graphs and maps. Epidemiological data are given for the various districts of West Bengal individually and this system is to be extended into other States in due course.

An account is given of the administrative difficulties encountered in the control of the disease. Prominent among these are the lack of a proper intelligence service to notify the incidence of morbidity and mortality due to cholera, the absence of an epidemiological unit at state level, the non-existence or deficiency of environmental sanitation and the absence of any central Act for the control of communicable disease. Besides these administrative difficulties failure to control cholera in the endemic areas of India is partly due to technical difficulties and various lacunae in our knowledge relating to cholera infection and its epidemiology. These are discussed in considerable detail, as is also the problem of prophylactic immunization.

In conclusion, the author urges the necessity of establishing a fully-fledged commission at the national level with the necessary facilities and staff to attack the problem of cholera as a whole, including bacteriological, clinical, epidemiological and immunological studies to evolve better methods of treatment, control, prevention and finally of eradication. *G. Covell*

Seal, S. C. in collaboration with A. L. Saha, B. Mukherju & A. Ghosh-Hazra. **Cholera in Greater Calcutta.** *Ibid.*, 29–42, 3 maps & 1 chart.

This is an appendix to the comprehensive report by Dr. Seal abstracted above. Cholera is prevalent throughout the area of greater Calcutta, which consists of 33 municipalities in addition to that administered by the Calcutta Corporation. These are situated on both banks of the Hooghly River from about 30 miles north to 16 miles south of the city proper.

Data are presented relating to the incidence and mortality from cholera in the various wards, from which it is concluded that variations in the prevalence of the disease are attributable to differences in environmental sanitation such as housing, water supply, excreta and refuse disposal, drainage, dampness, fly-breeding, presence of frankly polluted ponds and tanks and the provision of cultural and other amenities. Overcrowding *per se* does not seem to play any significant role. *G. Covell*

ABOU-GAREEB, A. H. **On the Search of Vibrios in the Cattle Dung at Calcutta and a Bengal Village during the Inter-Epidemic Period of the Years 1958–59.** Reprinted from *Internat. J. f. prophylak. Med. u. Sozialhyg.* 1960, Feb., v. 4, No. 1, 2 pp., 1 fig.

During the period of increased prevalence of cholera in 1958–59 the author observed, in West Bengal and in Nepal, that cholera was commoner in localities where cattle were numerous; many of the patients had had close association with cattle. It was also noticed that cattle dung was used as fertilizer, fuel cakes and (in solution) to sweep kitchens: the danger of contamination of hands and foodstuffs was therefore considerable.

He therefore collected 14 samples of fresh dung from 7 animals in a cattle shed in Calcutta, 10 samples from street cattle in the same city and 29 samples in a village at Singur, Bengal, before any confirmed cases of cholera appeared there. These samples were examined by conventional methods.

From 18 of the 53 samples, strains of vibrios were isolated. None of them "agglutinated O cholera serum" [*sic*] which had a proved titre of 500 against stock Inaba and Ogawa strains isolated from patients in Calcutta. They were all also negative to the haemolytic test. All 18 strains were classified by Heiberg's scheme and 6, 5, 3, 2 and 2 respectively were found to belong to Heiberg's groups I, II, III, V and VI. *H. J. O'D. Burke-Gaffney*

NIKONOV, A. G., KHOKHLOVA, A. M., BICHUL, K. C. & TIMOFEEVA, R. I. **Cholera Phage.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 1, 118–26. [Translated from Russian.]

Long continued propagation of the specific cholera phages in broth cultures of *Vibrio cholerae* was found to be unsatisfactory; the phage titres were always too low—not more than 10^4. Propagation in preparations of bile, however, was found to increase the lytic activity of the phages very considerably. Use of the ligated intestinal-loop technique of DE and CHATTERJE [this *Bulletin*, 1954, v. 51, 581] for the propagation of the phages also led to the development of phage preparations of very high activity and in many experimental infections in guineapigs the vibrios disappeared completely. *H. J. Bensted*

FORMAL, S. B., BOHNER, H., SCHNEIDER, H. & BARON, L. S. **Virulence of a Nutritional Mutant of *Vibrio comma*.** *Proc. Soc. Exper. Biol. & Med.* 1960, Feb., v. 103, No. 2, 359–61.

It was shown by BACON *et al.* [*Bull. Hyg.*, 1951, v. 26, 936] that purine-requiring mutants of *Salmonella typhi* injected intraperitoneally into mice are less virulent than their normal parents. Similar observations have been made by others and in view of the fact that laboratory strains of cholera vibrios differ in their capacity to kill mice it was decided to study the purine requirements of different strains of these organisms.

One strain required only glucose and inorganic salts for growth, another strain required purines in addition to the minimal medium, while a third, a mutant of the previous strain, proved to be purine independent. It was found

that the mouse virulence of the strain which required purine was increased if purines were injected at the same time as the challenge organism. The purine-independent mutant was significantly more virulent than the parent strain which required purine. The ability to produce fatal infections in guineapigs by oral administration of lower doses of the purine-independent variant as compared with the parent strain was not noted. It therefore seems likely that the organism must possess attributes additional to those needed to infect mice in order to bring about a fatal infection in guineapigs *H. J. Bensted*

MISRA, S. B. & SHRIVASTAVA, D. L., with the technical assistance of S. SINGH. **Studies in Immuno-Chemistry of *Vibrio cholerae*: Part I—Localization of Antigens in the Cells.** *J. Sci. & Indust. Res.* New Delhi. 1959, Nov., v. 18C, No. 11, 209–12, 1 fig. [10 refs.]

Saline suspensions of growths of *Vibrio cholerae*, strain Ogawa, washed off agar slopes after 16–18 hours' incubation, have been subjected to various treatments with the object of disrupting the bacterial cell wall and the isolation of possible antigen fractions for further investigation.

Examination by the agar gel diffusion technique indicated that the vibrio cell contained at least 7 antigens. The antigen responsible for the α-line was heat-stable and appeared to be readily released from the bacterial cells. It seemed probable that this antigen was the polysaccharide fraction responsible for the usual serological reactions related to the vibrio cell, and since the major part of this antigen is situated near the surface of the cell it would tend to be released with even mild mechanical treatment. The antigens responsible for the other 6 lines appeared to be heat-labile; they could be demonstrated only after complete lysis of the cell, so it is probable that they are located more deeply in the cell.

This is a preliminary report only and the results of further studies may be expected. *H. J. Bensted*

BENYAJATI, C., KEOPLUG, M., BEISEL, W. R., GANGROSA, E. J., SPRINZ, H. & SITPRIJA, V. **Acute Renal Failure in Asiatic Cholera: Clinicopathologic Correlations with Acute Tubular Necrosis and Hypokalemic Nephropathy.** *Ann. Intern. Med.* 1960, May, v. 52, No. 5, 960–75, 2 figs. [31 refs.]

The authors, working in Bangkok, Thailand, have investigated the mechanism of acute renal failure in 13 patients out of a series of 134 examples of the acute disease due to the Ogawa serotype of *Vibrio cholerae*, which occurred in an epidemic in February–March 1959. 5 patients came to autopsy.

Therapy was based on rapid rehydration with intravenous normal saline, acidosis was corrected by additional infusions of sodium lactate or bicarbonate, but potassium supplements were not generally given.

Autopsy demonstrated that renal failure was due to acute tubular necrosis in every case, while several patients showed hydropic or vacuolar degeneration of renal tubular cells typical of hypokalaemic damage as an additional lesion. Minimal changes were found in the glomeruli, and cortical necrosis was not

found, nor was the limited proximal tubular necrosis which is characteristic of acute toxic damage encountered. The authors conclude that renal failure in cholera is due to anexia from failure of renal blood flow, not to toxaemia, and that pre-renal azotaemia plays no part in the production of the clinical state.

During acute cholera the daily loss of potassium in the faeces may average 131 mEq., and routine replacement therapy did not take this into account [see also this *Bulletin*, 1960, v. 57, 808]. This would explain the absence of hyperkalaemia during acute renal failure in cholera patients, and also the hydropic and vacuolated degeneration of the renal tubular cells which was found as an independent pathological entity in several of the autopsy specimens. To combat this the authors suggest that in the presence of continuing diarrhoea, once the initial fluid replacement has been achieved, 10–20 mEq. of potassium should be added to each litre of maintenance fluid which is infused.

In patients who are severely shocked on admission, acute renal failure should be recognized by failure of urine flow to begin within an hour or two of rehydration, or of a scanty production which fails to reach 0·5–1 ml. per minute. In such cases the infusion of maintenance fluid and electrolytes must be carefully controlled in order to avoid hypervolaemia and death from acute pulmonary oedema. The duration of anuria in acute choleraic renal failure cannot be anticipated: in the present series it lasted from 3 to 10 days in patients who recovered, and for 18 and 20 days in 2 fatal cases.

[This is a well-illustrated, well-documented article which should be read in the original by all those concerned in the treatment of cholera.]

J. H. Walters

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

LAMY, L. Intérêt de l'utilisation de milieux de composition différente pour la culture des protozoaires parasites. Cas particulier de *Entamoeba histolytica*, *Trichomonas vaginalis* et *T. foetus*. [**Importance of the Use of Various Media for Cultivation of Parasitic Protozoa**] *Ann. Inst. Pasteur*. 1960, May, v. 98, No. 5, 761–5.

In maintaining parasitic protozoa whether *in vitro* or *in vivo* there appears to be a set of conditions in each case which is indispensable for continued survival. The author has made some observations on this subject especially with respect to protozoa which live in association with bacteria. In general he has used for protozoa of the alimentary and urinary tract media similar to that described by DOBELL and LAIDLAW [this *Bulletin*, 1927, v. 24, 363].

The general experience with fresh isolations is that there is a gradual decline in numbers on subculture, or even failure to multiply from the start. A culture

which continues to multiply regularly from the start is rarely obtained. It is not always clear whether the failure is due to the poor growth of the protozoa themselves or of the accompanying bacteria. The author describes 3 variations in medium of biphasic character having either coagulated horse serum or egg white as base in combination with rice starch. He finds that addition of vitamins, sugars or salts is unnecessary. In general parasites whose growth has been stabilized in one culture medium can be maintained with equal ease in a medium of similar composition which may however have failed to support growth during initial isolation. Special recommendations are made with regard to *Trichomonas* and *Entamoeba histolytica* cultures.

The media described may be used diagnostically where limited maintenance is required, for isolation and unlimited maintenance and for experiments in the laboratory under defined conditions. *J. D. Fulton*

i. SCHNEIDER, C. R. & PORTER, R. J. **Gamma Ray Effects on Trophozoites of *Entamoeba histolytica*.** *Exper. Parasit.* New York. 1960, Apr., v. 9, No. 2, 83–6, 3 figs.

ii. ——. **Radiosensitivity of *Entamoeba histolytica* Cysts.** *Ibid.*, 87–91, 1 fig.

i. Very few experiments have been recorded on the effect of radiation on amoebae. The earlier work of SADUN *et al.* [this *Bulletin*, 1951, v. 48, 261] on the effect of X-ray upon growth and infectivity of *Entamoeba histolytica* has been extended in the present investigation. The amoebic cultures were exposed to gamma radiation from a cobalt-60 source in dosage "reported in terms of RAD (corresponding to 100 ergs per gram)". The strain of amoebae maintained on egg slants was accompanied by a mixed bacterial flora and did not form cysts in culture or infect guineapigs but engulfed red cells. The conditions for irradiation are described, and before the amoebae were subjected to the gamma rays bacteria were removed by washing. Multiple exposures were made over a 6-month period and after irradiation growth in each culture was followed by haemocytometer counts. Irradiation of trophozoites with more than 195,300 RAD prevented development in culture. The lag phase in cultures receiving 100,000 RAD or less was similar to those of non-irradiated controls, indicating a small range between completely effective and non-effective dosage.

ii. In determining the radiosensitivity of *E. histolytica* cysts a strain isolated by DOBELL [*ibid.*, 1931, v. 28, 705] was used. The source of gamma rays was that described above, namely cobalt-60. Cysts were harvested from Ringer-egg-Locke slants after 72 hours' culture, washed and suspended in Locke solution to give about 5,000 per ml. Exposure times ranged from 10–60 minutes and corresponded to 8,400 to 50,200 RAD. Calculations were made to determine survival rates after radiation. When cysts of different ages were used trophozoites were eliminated from cultures by adding water and leaving overnight at 4–6°C. The data obtained suggested that difference in age of cysts of 24 hours did not affect susceptibility to irradiation. Cysts appeared to be much more sensitive than trophozoites to irradiation. Possible reasons for this variation in susceptibility are given, and it was established that doses of approximately 16,700 RAD completely destroyed almost all cysts.

J. D. Fulton

WEBSTER, B. H. **Pleuropulmonary Amebiasis. A Review with an Analysis of Ten Cases.** *Amer. Rev. Respiratory Dis.* 1960, May, v. 81, No. 5, 683–8. [18 refs.]

Among 249 patients with microscopically proven intestinal amoebiasis none had been out of North America and only 4 had had dysentery. Yet 48 had hepatic amoebiasis, and 10 were found to have pleuro-pulmonary amoebic complications secondary to it. The ages of the patients ranged from 36 to 82 years; all the 10 with lung involvement were white. Cough and slight fever were present in all 10; right side chest pain, wheezing and cardiac arrythmia were evident in 8 of them; and haemoptysis occurred in 6. In 9 the liver was palpably enlarged and in 8 tender; X-ray examinations showed raising and fixation of the right diaphragm in 7 patients, and adjacent lung changes in 6. Vegetative amoebae are said to have been recognized in the sputa of 9 patients and, it is claimed, "*Endamoeba histolytica* cysts were found exclusively in one case". Bile was present in the sputum of 8 patients.

Drugs used in treatment were chloroquine, alone or with Milibis, in 6 patients; diiodohydroxyquinoline glycolylarsanilate in 3 patients; and emetine hydrochloride only in one patient. In all cases the results were uniformly satisfactory, and no relapses followed.

[The finding of parasites in the sputum of every patient is indeed most unusual. The report of cysts alone, in the sputum of one of these patients, is remarkable. Such claims, in the absence of substantial verification, inevitably raise certain doubts of a fundamental nature.] *A. R. D. Adams*

ISLAM, N., ALAM, K. S. & QUADERI, M. A. **Hepatic Amoebiasis.** *J. Trop. Med. & Hyg.* 1960, June, v. 63, No. 6, 131–7, 6 figs. [12 refs.]

This is a report on 50 patients in a Dacca hospital, east Pakistan, with hepatic amoebiasis. In only 8 were parasites found in the stools. None of the patients was under 10 years of age—but the authors did not deal with children; the highest incidence (40%) was in the third decade; 10 (20%) were in the fourth decade of life; and 14 (28%) patients were in the fifth. The oldest patient was 80 years of age. All but 9 (18%) were males.

Right lower chest pain was an invariable symptom; fever was evident in 40 and cough in 28 patients. Cough may be due to diaphragmatic irritation or to lung extension of the liver lesion. The liver was palpably enlarged and tender in 42 patients, and there was fullness or oedema of the chest wall in 15 patients. Radiological changes were seen in 38 of the 48 patients examined by X-ray. Aspiration of liver lesions in 12 cases yielded parasites from only one of them; aspiration is not essential to diagnosis but it may be helpful in the treatment of selected cases. Cough with expectoration in a case of hepatic amoebiasis should suggest a search for liver cells in the sputum; these are certain evidence of pulmonary extension of the infection. Pneumoperitoneal inflation sometimes may help in diagnosis.

There are clinical details of 3 illustrative cases and some excellent X-ray and post-mortem photographs. *A. R. D. Adams*

MACDOUGALL, Lorna G. **Amoebiasis and its Complications in African Infants.** *East African Med. J.* 1960, Apr., v. 37, No. 4, 279–88.

At the King George VI Hospital, Nairobi, between July 1957 and September 1959, of 17 child in-patients admitted for treatment of amoebiasis 10 were found to have amoebic liver abscesses and others extra-intestinal amoebic complications; 9 of these died. All the 10 children with complicated amoebiasis were under 2 years of age; the remaining 7 children, who suffered no complications, were between 2 and 10 years of age.

Details are given of each of the 10 children suffering from grave complications; these took the form of multiple liver abscesses, pneumonitis, pleural effusions, empyema, subphrenic abscess, perforation of the gut, intussusception and peri-anal cutaneous amoebiasis. In all cases the diagnosis was confirmed by identification of vegetative *Entamoeba histolytica* in the affected tissues; post-mortem examinations were made in 8 cases.

In this series of cases bloody diarrhoea followed by liver enlargement were the usual initial manifestations. 3 of the children were entirely breast-fed and it was assumed, as usually is the case, that bacillary dysentery was the causative disease. In later cases the correct diagnosis was suspected earlier, but the condition of the children even then was too advanced for effective treatment. It is evident that amoebic dysentery, and its grave complications, are more prevalent than has been thought in African infants. Dysentery with hepatomegaly and respiratory and abdominal disorders in African children must be considered as possibly of this origin.

[See also this *Bulletin*, 1959, v. 56, 441; and 1960, v. 57, 474.]

A. R. D. Adams

SCRAGG, Joan. **Amoebic Liver Abscess in African Children.** *Arch. Dis. in Childhood.* 1960, Apr., v. 35, No. 180, 171–6, 6 figs. [17 refs.]

Over a period of 7 years, from 1951, 53 patients with hepatic amoebiasis were seen in the paediatric department of the King Edward VIII Hospital, Durban, South Africa. The youngest was 8 weeks, the oldest 5 years; 17 were under 1 year, and 10 under 6 months of age. 23 recovered and 30 died; 33 (62%) had right lobe abscesses, 2 (4%) left, 5 (9%) at the junction of the lobes, and in 13 (25%) the abscesses were multiple. Only half the patients had a previous history of dysentery and 23% suffered from dysentery at the time of admission; parasites were recognized in the stools of only 13 (29%) of the 45 so examined. Fever (usually 102°–103°F.) was always evident; and tender liver enlargement usually so. Radiological examination proved less helpful in diagnosis than it proves in adults.

Aspirated pus initially was usually grey-green or grey-yellow, and only later (or at autopsy) did it become anchovy in colour; it was bacteriologically sterile in all but 4 of the 40 aspirations, and parasites were found in it ante mortem in only 8 (20%). The complications resultant on the liver infection included rupture into neighbouring organs in 5 patients (3 died); brain abscess in an infant of 5 months (found at necropsy); and jaundice in one child, in whom 2 large abscesses were found at autopsy to be causing biliary obstruction.

Treatment was by emetine injections for 10 days (one-eighth to one-quarter

grain daily) or oral chloroquine (0·5 gm. followed by 0·25 gm. daily for 15 to 21 days) and supportive treatment, with a tetracycline antibiotic and diido-hydroxyquinoline when there was active dysentery. Open surgical drainage was done in 3 cases in this series; but on reflection the author thinks that if it had been undertaken more frequently the mortality might have been lower.

[This paper adds to the list of well authenticated papers appearing within recent years which indicate that the incidence of complicated amoebiasis in infants and children is considerably greater than has hitherto been suspected or recognized. In conjunction with these it merits the very earnest consideration of those concerned with the treatment of children. (See this *Bulletin*, 1960, v. 57, 474; and MACDOUGALL, above).] *A. R. D. Adams*

VIZCARRONDO, E., DOMÍNGUEZ, A. & SÁNCHEZ ROMERO, G. La amibiasis hepática en el niño. **[Hepatic Amoebiasis in Children]** *Archivos Venezolanos Puericult. y Pediat.* 1959, Apr.–June, v. 22, No. 72, 131–49, 12 figs. [15 refs.]

The authors, from Venezuela, give details of hepatic amoebiasis in 4 children aged 1¼, 2½, 5 and 6 years. *Entamoeba histolytica* was found in the faeces in 2, at autopsy in 1 and was assumed because of response to specific treatment in the fourth. The clinical and laboratory findings are tabulated and there are 4 photographs and 2 photomicrographs and also 6 radiographs. 2 patients died and details of autopsies are given. Treatment is discussed: in the present cases various combinations of drugs including chloroquine, sulphonamides, antibiotics and (in 1 patient) emetine were used. *H. J. O'D. Burke-Gaffney*

BIAGI F., F., FRANCO-GÓMEZ, A., MARTUSCELLI Q., A. & NAVARRETE, F. Amibiasis cutánea en una lactante. **[Cutaneous Amoebiasis in an Infant]** Reprinted from *Bol. Méd. Hosp. Infantil.* Mexico. 1960, v. 17, No. 1, 57–61, 3 figs. [11 refs.]

The English summary appended to the paper is as follows:—

"A case of cutaneous amoebiasis of the genitalia in a female infant is reported.

"Comments are made on clinical characteristics, the importance of an early diagnosis, the possible ways of infection, and treatment."

BUONOMINI, G. & MIGNANI, E. Azione patogena sperimentale di E. histolytica. Rilievi preliminari sulla inoculazione in ratti e topi albini di trofozoiti o loro estratti. Aspetti anatomo-patologici. **[Pathological Effect of *Entamoeba histolytica*. Results of Inoculation of Rats and Mice with Trophozoites or their Extracts. Histopathological Aspects]** *Giorn. di Malattie Infettive e Parassit.* 1959, Nov., v. 11, No. 11, 961–3, 6 figs.

In order to study the effect of *Entamoeba histolytica* on organs other than the intestine, the authors inoculated rats and mice intravenously with washed

cultures and cryolysed amoebae. In rats neither the amoebae nor their cryolysates produced any changes, but most of the mice died within 24 hours. On the other hand, inoculation of the concomitant bacteria or their cryolysates caused no damage to these rodents. The autopsy of the animals that died revealed pathological changes in the blood vessels (haemorrhagic broncho-alveolitis), lymph nodes (necrotic hyperplasia) and liver (perilobular hepatitis). The trophozoites showed a special predilection for the intestinal wall, the penetration of which—with ulceration—was apparently facilitated by hyperplasia and necrosis of the intestinal lymph nodes. The histopathological changes are depicted in a number of photomicrographs. *C. A. Hoare*

LUMBRERAS, H., WESTPHAL, A. & FLORES, W. Über den Mechanismus der *in vitro*—Wirkung des Oxytetracyclins und des Tetracyclins auf *Balantidium coli*. [**Mode of Action of Oxytetracycline and Tetracycline on** *Balantidium coli in vitro*] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1959, Dec., v. 10, No. 4, 361–71. [21 refs.]

Experiments on the action of chlortetracycline *in vitro* on *Balantidium coli* were reported by AGOSIN *et al.* [this *Bulletin*, 1951, v. 48, 156]. It appeared that the action was direct and not on added microflora. The present authors have made similar studies with oxytetracycline and tetracycline.

The parasite was generally maintained in a fluid medium consisting of horse serum and egg white in Ringer solution with the addition of starch. The drugs were studied in concentrations ranging from 1/2000 to 1/10,000 and the *p*H range varied between 4·5 and 7·0. It was clear that the presence of bacteria played an important part. After the drug had acted for a definite period samples of sediment were inoculated to fresh medium and survival studied. It was found that survival in presence of 1/2000 oxytetracycline was 48 hours and 144 hours when the lowest concentration was used. Addition of bacteria at regular intervals increased the life span of *B. coli* which had been in contact with antibiotic.

The role of bacteria when the above parasite was in contact with 1/5000 of either drug suggested that there were three phases of antibiotic activity: (1) a bacteriostatic phase in which *B. coli* will recover on transfer to fresh medium, (2) a bactericide-parasitostatic phase in which recovery of the ciliate is still possible, and (3) a parasiticidal phase in which life of *B. coli* may be prolonged but there is no recovery.

A report on the effect of the above 2 drugs on *B. coli* was also made by DE CARNERI [*ibid.*, 1960, v. 57, 37]. *J. D. Fulton*

RUIZ, A. & ALFARO, M. *Retortamonas intestinalis* (Wenyon et O'Connor) en Costa Rica. [*Retortamonas intestinalis* **in Costa Rica**] *Rev. Biologia Trop.* San José, Costa Rica. 1959, Dec., v. 7, No. 2, 231.

Report of a case.

RELAPSING FEVER AND OTHER SPIROCHAETOSES

LAPIERRE, J., ROUSSET, J. J. & PICOT, M. Sensibilité du Hérisson (*Erinaceus europaeus*) à différentes espèces de *Borrelia*. [**The Susceptibility of the Hedgehog (*Erinaceus europaeus*) to Different Species of *Borrelia***] *C.R. Soc. Biol.* 1960, v. 153, No. 11, 1718–20.

The authors inoculated hedgehogs, from the west of France, with five strains of *Borrelia*: a strain of *B. duttoni*, isolated near Lake Albert; two strains of *B. crocidurae*, from Dakar; a strain of *B. hispanica* maintained at the Institut Pasteur, Paris; and a strain of *B. persica* from Kurdistan. The strains had been maintained either in ticks or by direct passage in mice. The hedgehogs were inoculated either intraperitoneally or intramuscularly with blood containing spirochaetes.

9 hedgehogs inoculated with varying doses of *B. duttoni* showed no signs of infection either in the blood or brain. On the other hand out of 7 inoculated with *B. crocidurae* 3 developed inapparent infections although spirochaetes were not seen in the blood. 3 animals inoculated with *B. persica* showed visible spirochaetes in the circulation and their blood was infectious to mice. A single hedgehog inoculated with *B. hispanica* developed a characteristic infection, as previously recorded by BRUMPT [this *Bulletin*, 1950, v. 47, 573].

Edward Hindle

WALTON, G. A. **The Reaction of Some Variants of *Ornithodoros moubata* Murray (Argasidae, Ixodoidea) to Desiccation.** *Parasitology*. 1960, May, v. 50, Nos. 1/2, 81–8, 2 figs. [15 refs.]

This is a further extension of the work previously reported [this *Bulletin*, 1958, v. 55, 895 and 1014] in which 4 biological variants of *Ornithodoros moubata* were recognized in East Africa and designated A, B, C and D. A form E, domestic and from South Africa, was later proposed [*ibid.*, 1960, v. 57, 130] and a further East African wild form (F) has been nominated differing in certain respects from the other wild form C.

These forms, and one hybrid, were kept in tubes at 32·2°C. in a constant temperature room and in closed chambers in dry air over pure sulphuric acid to test their resistance to desiccation. Each strain was represented initially by 20 females, unfed, unmated and within one month of moulting from the last nymphal stage. Dead ticks and excrements were not removed. Weighings were made every third day and, since nothing was discarded, losses in weight represent loss of water.

The experiments were continued until mortality was 100% in one of the series and this was of form B—from huts in a hot, low coastal area near Mombasa and addicted to feeding on chickens rather than man. All these form B ticks died in 96 days. Other forms by this time were often still mainly alive, ranging up to 90% alive in a South African domestic form (E). There are replicate experiments for some forms, each " replicate " being of ticks from a different hut or locality within the range and conditions deemed characteristic of the form. These are referred to as strains of the forms. It may be noted that strains of the same form did not always survive equally long (*e.g.* the survival

of three A strains is 65%, 60% and 5%; for two E forms—less discrepant—75% and 90%), but survival is related to the initial weight of the ticks. The larger ticks survive longer and size alone may make, it is estimated, a difference of two months in the survival of ticks of the same form. Elsewhere [*ibid.*, 1958, v. 55, 1014] resistance to starvation at 85% RH, after a single blood meal, is shown to differ widely between the East African domestic forms A and B, in contrast to the wild form F. About 40% deaths of the domestic forms occurred within 9 months (A) and 18 months (B), but this mortality was not reached with wild F for 4 years 8 months.

All the East African forms, whether domestic (A, B and D) or wild (C and F), lost 0·32 mgm. water per tick daily, but the South African domestic (E) lost water at half this rate, *viz.* 0·16 mgm. per day. *D. S. Bertram*

LEPROSY

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control.

De Souza Lima, L. **Leprosy in the Americas.** *Internat. J. Leprosy.* Wash. 1960, Jan.–Mar., v. 28, No. 1, 50–65. [Refs. in footnotes.] [Translation from *Bol. Oficina Sanitaria Panamericana.* 1958, v. 45, 472–93.]

[See this *Bulletin*, 1959, v. 56, 629.]

Imaeda, T. **Electron Microscopic Analysis of the Components of Lepra Cells.** *Internat. J. Leprosy.* Wash. 1960, Jan.–Mar., v. 28, No. 1, 22–37, 7 figs. [25 refs.]

The object of this study was to find out the mechanism of formation and the composition of the opaque droplets and foamy structures in the lepra cell. In electron staining neither saturated fatty acids nor cholesterol exhibit an osmiophilic property and cause hardly any scattering of the electron beam: but unsaturated fatty acid and its ester, neutral fat, show intense electron staining. Phosphatides containing unsaturated fatty acids show moderate electron density.

There are three theories as to the origin of lipid substances in lepra cells: that they are pinocytotic droplets from the surrounding fat, that they are reactive products of the cytoplasm, that they are degenerative products of the bacilli. The author upholds the first of these opinions, but from his studies with electron staining considers that the pinocytotic droplets do not consist of neutral fat, but are lipoprotein derived from the blood stream, and are in the form of a hydrophilic colloid deposited around bacilli. It is supposed that the foamy, structure is the terminal appearance of the opaque droplet, and that

it may contain saturated fatty acids or their derivatives. The electron-transparent zone around the leprosy bacilli may be an aqueous phase in which various metabolites of the bacilli are dissolved.

The article is illustrated with 7 electron microscopic photographs.

[See also this *Bulletin*, 1959, v. 56, 447.] *Ernest Muir*

Weiss, D. L. & Fusillo, M. H. **Lack of Reactivity to Tuberculous Antigen of Leprosy Sera as assayed by the Globulin Titration Technique.** *Internat. J. Leprosy.* Wash. 1960, Jan.–Mar., v. 28, No. 1, 47–9, 1 fig.

When 56 leprosy patients (11 with lepromatous leprosy and amyloidosis, 2 with erythema nodosum, 29 with active lepromatous leprosy, 8 with arrested lepromatous, and 6 with inactive tuberculoid leprosy) were treated with the globulin titration technique [*Bull. Hyg.*, 1958, v. 33, 171 *bis*], no circulating antibody comparable to that demonstrated in active tuberculosis could be demonstrated. In only 10 of these leprosy patients was the antistreptolysin titre negative, and 4 of these were bacteriologically positive. From this study it is considered that the antigenic mosaic of *Mycobacterium leprae* is not related to that of *Myco. tuberculosis* with respect to the stimulation of a comparable circulating antibody globulin as measured by the globulin titration technique.

Ernest Muir

McFadzean, J. A. **Tuberculosis and Leprosy. Cross Desensitization between Tuberculin and Lepromin.** *Internat. J. Leprosy.* Wash. 1960, Jan.–Mar., v. 28, No. 1, 44–6.

If BCG converts a lepromin-negative person to a positive reactor, then will desensitization to tuberculin convert a positive lepromin reactor to a negative one? To answer this question 2 patients with positive reactions to both tuberculin and lepromin, and suffering from tuberculoid leprosy, were desensitized to tuberculin, injections of 10 rising to 5,000 TU being given. It was found however that their lepromin reactions, at readings after 72 hours and after 21 days, remained the same as before desensitization. An attempt to desensitize 2 similar patients by injection of bacterial powder of *Mycobacterium leprae* resulted in sterile abscesses "and anomalous skin reactions were subsequently obtained". *Ernest Muir*

Azulay, R. D., Cezar de Andrade, Lygia M., Silva, C., Rabelo Netto, A. V., Azulay, J. D., Neves, R. G. & Alonso, A. M. **Comparison of the Macroscopic Readings and Microscopic Findings of the Lepromin Reaction.** *Internat. J. Leprosy.* Wash. 1960, Jan.–Mar., v. 28, No. 1, 38–43. [17 refs.]

The object of the work described in this paper is to compare the clinical readings of the Mitsuda reaction (by using the Madrid Congress criteria) with the histological appearances, and particularly with the presence of the tuberculoid granuloma, in patients with arrested lepromatous disease. After examination histologically of the sites of 94 lepromin tests the authors found that 8

(38%) of 21 clinically doubtful reactions showed tuberculoid granuloma; that 18 (25%) of 71 clinically positive reactions did not present tuberculoid granuloma; that of 13 clinically doubtful reactions in arrested lepromatous cases 3 showed tuberculoid granuloma; and that 14 (54%) of 26 positive reactions in arrested lepromatous cases showed tuberculoid granuloma. The authors conclude that their findings are against Rotberg's "anergic-margin" theory, according to which lepromatous leprosy arises from the anergic margin of subjects because of their inability to produce the tuberculoid granuloma.

[See also this *Bulletin*, 1957, v. 54, 1194.] *Ernest Muir*

Languillon, J., Boissan, R. & Picart, P. La C réactive protéine dans la maladie de Hansen. [**C-Reactive Protein in Hansen's Disease**] *Méd. Trop.* Marseilles. 1960, May–June, v. 20, No. 3, 365–7.

Reference is made to the work of Tillet and Francis [*Bull. Hyg.*, 1931, v. 6, 212] who showed that the serum of patients with acute pneumonia precipitated with the polysaccharide C of the pneumococcus. After testing the sera of 156 lepromatous, 142 tuberculoid and 40 undifferentiated cases of leprosy, the authors found lower rates than had been found by American workers [see this *Bulletin*, 1960, v. 57, 135], and concluded that C-reactive protein (CRP) is an indication not of leprosy but of an inflammatory state. It is found more frequently in the lepromatous type of leprosy (37·8%) than in the tuberculoid (19%), and particularly when patients with the lepromatous type of the disease are suffering from lepra reaction. CRP diminishes with the favourable course of reaction, and if it remains at a high level a relapse of lepra reaction is to be expected. *Ernest Muir*

Doull, J. A. **Current Status of the Therapy of Leprosy.** [Report to the Council on Drugs (Kautz, H. D., Secretary).] *J. Amer. Med. Ass.* 1960, May 28, v. 173, No. 4, 363–73. [21 refs.]

In the absence of cultivation of *Mycobacterium leprae* on artificial media and transmission to animals, the action of drugs on other pathogenic mycobacteria that can be cultivated and transmitted to laboratory animals has to be studied as a substitute. Advantage has been taken of information gained in "screening" drugs against *Myco. tuberculosis* and in treatment of human and experimental tuberculosis, though analogy with tuberculosis has failed in many instances.

The Report gives a short review of the chemical formulae of sulphone drugs, of the incidence of leprosy, of the classification of types of leprosy. It then goes on to describe the evaluation studies of the Leonard Wood Memorial as recounted in the *International Journal of Leprosy* [this *Bulletin*, 1955, v. 52, 1097; 1958, v. 55, 1128].

After a brief reference to older forms of therapy, the sulphones are dealt with in detail as regards their history, pharmacology, toxicity in animals, inhibitory capacity against mycobacteria, effectiveness in experimental tuberculosis and other mycobacterial infections, and clinical use in leprosy.

Sulphones are considered to be the drugs of choice in the treatment of leprosy, DDS the parent sulphone giving the same results as disubstituted compounds, though a few patients tolerate the latter better. The author considers that "In active tuberculoid cases with multiple lesions, sulfones should be given, although evidence of their value is not conclusive" [a point of view which very few experienced leprologists would support].

The use of other drugs and antibiotics and non-specific vaccine therapy are discussed.

The treatment of the reactions of leprosy is next dealt with, as is the treatment of other complications, special reference being made to lesions of the eye.

The basic needs are: a method of cultivation of the leprosy bacillus and an animal that is susceptible to the disease. "Every drug or antibiotic that shows significant action against any mycobacterium and is proved safe according to long-term toxicity studies should be tested in leprosy in humans."

Ernest Muir

Doull, J. A., Rodriguez, J. N., Tolentino, J. G. & Fernandez, J. V. **Clinical Evaluation Studies in Lepromatous Leprosy: a 24-Weeks' Study of Pyrazinamide-Isoniazid Therapy.** *Internat. J. Leprosy.* Wash. 1960, Jan.–Mar., v. 28, No. 1, 12–17. [10 refs.]

Because of their activity in tuberculosis and in rat leprosy, the authors tested the use of a combination of pyrazinamide (PZA) and isoniazid (INH) in the treatment of 15 lepromatous patients at each of 2 leprosaria in the Philippines. Only 9 of the patients had had previous sulphone treatment. Matched against these was an equal number of patients on DDS as controls. Treatment lasted for 24 weeks.

Of the 26 test patients who finished treatment 6 showed clinical improvement compared with 9 in the DDS group; 13 remained stationary compared with 16 on DDS, and 7 became worse compared with 1 in the DDS group. Bacteriologically no change was noted in either group. The dosage used was 30 mgm. of PZA per kgm. body weight, and 5 mgm. per kgm. of INH.

Ernest Muir

Doull, J. A., Rodriguez, J. N., Tolentino, J. G. & Fernandez, J. V. **Clinical Evaluation Studies in Lepromatous Leprosy: a 48-Weeks' Study of Cycloserine Therapy.** *Internat. J. Leprosy.* Wash. 1960, Jan.–Mar., v. 28, No. 1, 18–21. [13 refs.]

Cycloserine, an antibiotic produced by *Streptomyces orchidaceus*, was compared with DDS, 14 leprosy patients being treated with the former, and 18 with the latter over a period of 48 weeks. Of those on cycloserine 4 showed clinical improvement, while of those on DDS 14 showed improvement. There was no significant sign of greater bacteriological improvement in one form of treatment compared with the other. Cycloserine was well tolerated.

Ernest Muir

DAVEY, T. F. **Some Recent Chemotherapeutic Work in Leprosy: with a Discussion of some of the Problems involved in Clinical Trials.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, May, v. 54, No. 3, 199–206, 12 figs. (8 coloured) on 3 pls. Discussion 207–11 [REES, R. J. W.; DRIVER, G. W.; JOPLING, W. H.; RIDLEY, D. S.; CHATTERJEE, K. R.].

The main part of this paper is concerned with the results obtained by the author in the trial of two drugs in the treatment of leprosy, namely Ciba 1906 and Etisul. But before describing these he shows the present position in regard to sulphone treatment, the need for alternative drugs, and certain problems incidental to the discovery of new and more effective chemotherapeutic agents. To compete with DDS a new drug must be acceptable to patients, be eminently free from toxic action, be at least comparable in activity with DDS and capable of use in combination with that drug, and for mass use it must be of low cost.

4 problems arise in the search for such new drugs, which are associated with bacteriology, immunology, classification and the selection of patients.

(1) *Bacteriology*. It is not known whether what is called *Mycobacterium leprae* is the same organism or the same strain throughout the world. The response to drugs may vary with the length of time that the infection has been in the body. In assessing the diminution in numbers of bacilli under treatment, it is to be remembered that the numbers vary tremendously in different parts of the body, so that considerable experience is needed in selecting sites for taking specimens for examination. The morphology of the bacilli may have an important bearing on drug trials, granular bacilli showing a stage in resolution.

(2) *Immunology and Classification*. "Any drug possessing antibacterial activity against *M. leprae* will be effective in all forms of active disease, but progress may be considerably influenced by the capacity of the body to induce spontaneous improvement quite apart from chemotherapy."

(3) The third set of problems is associated with the choice of patients. It is important to know if patients have had previous treatment. As leprosy control develops patients go to institutions less for treatment of the disease itself and more for the care of complications, and it thus takes a long time to assemble suitable comparable groups. It is necessary to create confidence in the patient that those who are conducting the trials have his interests as their first concern. Using DDS as a standard it is wise to match controls as accurately as possible, especially in small pilot trials, though in larger trials random selection may be used. "We have found it helpful to use as a control where Bacterial Index is concerned, not individual controls, but accumulated experience with large numbers of patients who have received DDS treatment, constructing a graph showing the average alteration in Bacterial Index with the passage of time of as many bacteriologically positive cases as were available. This procedure eliminates the necessity for individual controls and provides a standard against which one new drug can be compared with another."

Reports on trials with Ciba 1906 have already been published [this *Bulletin*, 1956, v. 53, 1435; 1958, v. 55, 524]. "Up to the 36th month the group decline in Bacterial Index among patients in the pilot trial continued to be better than the DDS standard. Between the 36th and the 44th month, however, progress was halted in six patients, with the reappearance in each case of bacilli of normal morphology, and in two cases an eruption of fresh skin lesions." Also 3 discharged patients returned with reactivation. It is therefore necessary to

combine Ciba 1906 with DDS. Its main usefulness is in the earlier phases of treatment when its freedom from toxicity makes it unnecessary for the therapeutic dose to be built up gradually, a full dose of 2 gm. daily being given to the adult.

Etisul (*diethyl dithiolisophthalate*). This drug, which is administered by inunction, has already been reported [*ibid.*, 1959, v. 56, 542, 1146]. Its action appears to be exerted mainly on bacilli of normal morphology, and it appears to have little action once the bacilli have become granular. In a course of Etisul lasting 8 to 12 weeks followed by standard sulphone treatment there was very good progress, though this was slowed up during the second 3 months while the DDS dosage was being built up; the subsequent progress was in advance of the DDS standard.

It is acknowledged that neither of these drugs meets the need for a single basic, non-toxic, rapidly effective antileprosy remedy, though they both have a useful place in leprosy treatment.

There is urgent need for closer contact between leprologists engaged in this work, and " A continuing Chemotherapeutic Panel of the International Leprosy Association would have a most valuable function in standardizing techniques, advising on the organization of trials, encouraging unity in clinical assessment, and in analyzing sources of difference in findings between one country and another ".

In the discussion which followed the reading of this paper Rees suggested that the application or modification of some of the methods used in tuberculosis since the war may be helpful in leprosy; that the number of patients available for trials could be increased by " widely dispersed centres taking part in a centrally controlled trial, and broadening the types of leprosy admitted. The obvious difficulty of including different types of leprosy to the trial could be overcome by matching, clinically and histologically, pairs of patients and distributing them at random between the two treatment groups ". He suggested an outside observer for assessing clinical progress in leprosy trials. He confirmed Davey's suggestion that irregular staining with granularity is more sensitive than the bacterial index in assessing improvement, by reference to corresponding trials in rats treated with isoniazid. He also found that the bacilli which stain irregularly are the same bacilli which show degenerate changes in the electron microscope.

Driver mentioned that, in seeking an acceptable compound from ethyl mercaptan, Etisul had been chosen from 400 derivatives; that Etisul has no cross resistance with the other anti-mycobacterial drugs, and it is very effective against murine leprosy. Its antituberculosis action is due to the release of ethyl mercaptan in the body, but neither compound shows any antituberculosis action *in vitro*.

Jopling referred to his failure to get favourable results with Etisul in 4 cases, and thought that this might be due to the bacilli already being dead as shown by the fact that all the bacilli were granular at the time of the beginning of treatment. He also expressed a hope that an effective analgesic might be found, safe and free from side effects, for the treatment of pain in leprosy.

Ridley mentioned that experiments on monkeys showed that dead bacilli took as long to absorb as living ones. " Chemotherapy we hope kills bacilli, stops the progression of the infection and prevents relapse; but after that it

could be that the destruction and removal of bacilli, on which so much depends, is left to the patient's own efforts."

Chatterjee referred to the possibility of there being different strains of *Myco. leprae* as shown in morphological features by the electron microscope.

[For anyone in a position to carry out trials on antileprosy drugs this paper is one of considerable value.] *Ernest Muir*

MONTESTRUC, E. & BENOIST, J. Action bactériologique du *p*-N, N-diméthyl-aminophényl-I *p-n*, butoxyphényl-3 thio-2 urée sur les lèpres du type lépromateux et dimorphes sulfono-résistantes. [**The Bacteriological Action of *p*-N, N-Dimethylaminophenyl-1 *p-n* Butoxyphenyl-3 Thio-2 Urea (Ciba-1906) on Sulphone-Resistant Leprosy Patients of the Lepromatous and Dimorphous Types**] *Bull. Soc. Path. Exot.* 1960, Jan.–Feb., v. 53, No. 1, 13–16.

After referring to the results with Ciba 1906 obtained by previous workers [this *Bulletin*, 1957, v. 54, 1421; 1958, v. 55, 524], the authors describe their own results with 4 patients, 2 lepromatous and 2 dimorphous, chosen from a group who had not become bacteriologically negative on DDS during periods of 1 to 3 years. After initial lower doses the continuing dose was fixed at 3 gm. per day. This was well tolerated: only 1 patient had slight erythema without fever. The results were favourable, all 4 patients becoming bacteriologically negative within 6 months. It is considered that Ciba 1906 is of great use in patients who under sulphone or other treatment show a certain resistance of *Mycobacterium leprae* to that treatment.

Ernest Muir

BROWN, J. A. K. **The Role of Leprosaria and Treatment Villages in Mass Campaigns in Tropical Africa.** *Internat. J. Leprosy*. Wash. 1960, Jan.–Mar., v. 28, No. 1, 1–11, 5 figs. [11 refs.]

The author, who first started leprosy work in southern Nigeria in 1930, begins by describing the method gradually evolved there. This implied a leprosarium in each province, and a system of local clinics attached to special satellite villages in which the patients should live, one such special village to be created for each group of compounds.

The author goes on to describe his more recent work as leprosy specialist in Uganda. Whereas in southern Nigeria the people live huddled together in compounds and villages at nearly sea level, in Uganda there are no villages and at 4,000 feet the climate is more equable. In 1951 there were in Uganda, with its population of 5½ million, 70,000 leprosy patients of whom 9% were lepromatous. There were 5 leprosaria with accommodation for 2,000 patients and for treatment of a similar number of out-patients; most of these institutions were on the fringe of the country. It was calculated that the number of patients living within a radius of 20 to 25 miles from a treatment centre would be 635. Because of the nature of the country and the distribution of the population a policy was adopted of treatment villages linked, as far as possible, to leprosaria and supplemented by out-patient clinics. In the leprosaria, while the central

buildings are of more permanent structure, the patients' huts are generally of cheap temporary materials, as they are also in the treatment villages.

In the last 7 years 80 treatment villages have been built, each with its out-patient clinic, and there are now very few parts of the country where patients are without accommodation and treatment. Photographs are given showing the simple yet orderly nature of these treatment villages. Their location is determined by previously conducted surveys with examination of every person. One of the chief difficulties is to secure regular treatment, but this is much easier where patients have not to go a long distance to the treatment centre.

Under this scheme the leprosaria act as consulting hospitals; their 20 doctors and nurses give medical supervision to the treatment villages and clinics, and train the paramedical staff who are employed in them. In the villages treatment with DDS tablets is given twice weekly; in each there is accommodation for 50 to 100 patients; relatives are not admitted except where babies still require nursing. It is hoped that as leprosy diminishes these villages and clinics may be gradually closed down, until in the end leprosaria alone supply residential quarters. *Ernest Muir*

HELMINTHIASIS

*In this section abstracts are arranged as far as possible in the following order:—*TREMATODES *(schistosomes, other flukes);* CESTODES *(Diphyllobothrium, Taenia, Echinococcus, other cestodes);* NEMATODES *(hookworms, Ascaris, filarial worms, Dracunculus, etc., Trichuris, Enterobius, Trichinella, etc.).*

COWPER, S. G. & WOODWARD, S. F. **A Preliminary Note on Parasitic Infections on the Moor Plantation, Ibadan. A Study of One Hundred Employees.** *West African Med. J.* 1960, June, v. 9, (n.s.) No. 3, 123–30. [29 refs.]

This survey of 100 persons, selected at random from those working in the area of the Moor Plantation, 4 miles from Ibadan, Nigeria, occupied by the Regional Department of Agriculture, was intended to discover whether diseases such as schistosomiasis, loiasis and onchocerciasis are being transmitted locally. The intestinal parasites, helminthic and protozoal, were found to be very common. *Schistosoma haematobium* ova were found in the urines of 8 persons examined, and potential vector snails were found in the area. Skin snips were done on only 2 persons with suggestive skin conditions: both were positive for *Onchocerca volvulus*, and out of 100 locally caught *Simulium damnosum* 2 had microfilariae in their thoracic muscles. *Loa loa* infection was found in 4 persons: *Chrysops silacea* and *C. longicornis* have been caught in the area. It is concluded that there is at least circumstantial evidence for the transmission of schistosomiasis, loiasis and onchocerciasis in the area. Findings are shown in tables and figures. *B. B. Waddy*

MALDONADO, J. F. & OLIVER-GONZÁLEZ, J. **Intestinal Helminthiasis in Six Selected Areas of Puerto Rico.** *Amer. J. Pub. Health.* 1960, June, v. 50, No. 6, Pt. 1, 837–42. [16 refs.]

See this *Bulletin*, 1959, v. 56, 1284.

BARUFFA, G. Osservazioni sulla epidemiologia della schistosomiasi vescicale nel distretto di Gelib (Basso Giuba Somalia). [**Observations on the Epidemiology of Urinary Schistosomiasis in Gelib District (Low Juba, Somaliland)**] *Riv. di Parassit.* Rome. 1960, Mar., v. 21, No. 1, 1–12, 2 figs. [15 refs.] English summary.

During 1956 and 1958, the author examined 338 schoolchildren from 4 localities along the river Juba, in Somalia, and found vesical schistosomiasis affecting from 15 to 75% of the various groups: he discusses possible explanations for these variations in incidence. In another group of 145 persons of both sexes and all ages, he found ova of *Schistosoma* in the urine of 48%. 2 other groups of labourers were positive in 78% and 52% respectively. An occupational factor common to most of those affected was farming or other activities in contact with the flooded land or the irrigation channels.

Bulinus (*Physopsis*) *abyssinicus* is the vector of *Schistosoma haematobium* in Somalia and it is to be found in large numbers along the edges of the floods which seasonally spread from the banks of the river Juba during October-November, after the "big" rains of April-June, when rainfall may register up to 16–24 inches. *Nymphaea zanzibariensis* then grows in the flooded areas, producing edible seeds and bulbs which are gathered by women and children who also bathe in the flood waters. As the flood waters recede, fish are caught and the ground is next sown with sesame. The opportunities of infection of this population are obvious. The snail vector is not found in the river itself.

The author has interrogated 266 patients: 172 (62%) set the onset of their illness (haematuria) between December and May and he relates this to the life cycle of the helminth in the light of the known hydrological circumstances.

Mass treatment with such new drugs as TWSb (antimony dimercaptosuccinate) should achieve the eradication of schistosomiasis in spite of the survival of the snail vector, chemical control of which would cost too much.

J. Cauchi

WEBBE, G. **Observations on the Seasonal Fluctuation of Snail-Population Densities in the Northern Province of Tanganyika.** *Ann. Trop. Med. & Parasit.* 1960, Apr., v. 54, No. 1, 54–9, 1 fig. [11 refs.]

Many of the reports of seasonal fluctuations in the density of fresh-water snail populations are conflicting. Webbe has carried out weekly observations on a population of *Biomphalaria pfeifferi nairobiensis* in Tanganyika over a period of 18 months. The results show that there is a marked drop in the population density after the long rains (April–May) and that breeding is not resumed on a big scale until September. The short rains from October to December did not appear to have any adverse effect on breeding. The sampling techniques

employed consisted of the use of bamboo traps and hand-collecting. The author concludes that population studies should be carried out in as wide a variety of habitats as possible because the seasonal effects on a given species may vary from place to place.

[See also this *Bulletin*, 1958, v. 55, 536, 537, 539 ; 1959, v. 56, 170.]

C. A. Wright

RAE, M. Viola & JACKSON, W. S. T. **Bilharzial Appendicitis.** *Canadian Med. Ass. J.* 1960. June 18, v. 82, No. 25, 1270–72, 4 figs.

"A case of Bilharzial appendicitis in a young Greek mariner is reported. Lesions were present in various stages of development and the histological details are described.

"With widespread world travel, the occurrence of sporadic cases of infestation is an increasing possibility."

FOSTER, R., TEESDALE, C. & POULTON, G. F. **Trials with a New Molluscicide.** *Bull. World Health Organization*. Geneva. 1960, v. 22, No. 5, 543–8.

Tests with Molluscicide Bayer 73 (2-hydroxy-5,2-dichloro-4 nitro-benzanilide) against East African snails are described. In the laboratory a concentration of 0·5 p.p.m. was completely or partially ineffective according to snail species. At 1 p.p.m. kills were 85 to 100% according to species. As a result, in a field trial a continuous dosage of 1 p.p.m. for 12 hours was applied to a 4,000-yard stretch of river. Bamboo raft traps were placed at intervals, to attract snails and indicate their presence, for 3,100 yards below and (as a control) 900 yards above the dosing point. Snails and eggs disappeared completely from the treated section after the molluscicide application. By the following day searches beyond the trapped area revealed no snails for a further mile: thus the application was apparently effective for 3 miles beyond the dosing point. Chemical analyses showed that the spread of the molluscicide downstream was slow, but after 6–7 hours the concentration was 0·9 p.p.m. 1,500 yards downstream. [This seems to indicate that this compound does not readily decompose under field conditions, a disadvantage of sodium pentachlorophenate.] There was no tendency for snails to leave the water and avoid intoxication. There was evidence that the dosage of 1 p.p.m. was excessive in field conditions, and further trials with lower doses are planned. The makers' stated lethal limit to fish being 1 p.p.m., a lower dose would be advantageous. [In French experiments with DDT, fish fry were very much more susceptible than grown fish, and therefore application at a time of year avoiding the breeding season was considered important.]

Data are now available for 4 months after the application. In 13 searches only 67 specimens of *Biomphalaria pfeifferi nairobiensis* and 15 of *Bulinus tropicus* were found, mostly close below the dosing point and presumably washed down the river. But *Limnaea natalensis* repopulated the stretch, quite suddenly, after a month: it was apparent that this snail, though undetected for a time, had never been eliminated, a fact which throws some doubts on the present methods of search for snails.

B. B. Waddy

BARBOSA, F. S. & BARRETO, A. C. **Differences in Susceptibility of Brazilian Strains of *Australorbis glabratus* to *Schistosoma mansoni*.** *Exper. Parasit.* New York. 1960, Apr., v. 9, No. 2, 137–40. [12 refs.]

Two strains of the snail *Australorbis glabratus*, one from Salvador (Bahia, Brazil) and the other from Paulista, Pernambuco, Brazil, were exposed to the strain of *Schistosoma mansoni* from Pernambuco. Only 1·7% of the Salvador snails became infected while the other strain proved very susceptible. Comparison of the tissue reactions of the two strains of snail to the invading miracidia showed no reaction in the tissues of the susceptible strain but in the resistant forms most of the larvae were destroyed. No morphological differences could be detected between the two strains but eggs laid by albino Pernambuco snails which had been crossed with pigmented Bahian individuals showed reduced viability. The authors conclude that this evidence indicates that the differences in susceptibility to infection are due to the snails and not to the parasite. *C. A. Wright*

PRATA, A. & SILVA, P. Tratamento da esquistossomose mansônica pelo sulfato de 2-4-di-dietilamino-etóxi-desoxibenzoina. [**Treatment of *Schistosoma mansoni* Infection with Desoxybenzoin**] Reprinted from *Hospital.* Rio de Janeiro. 1960, Feb., v. 57, No. 2, 263–6.

The English summary appended to the paper is as follows:—

"The authors have treated 20 patients of schistosomiasis mansoni with desoxybenzoin, using 0·5 g tablets which contained 0·075 g of active basis. Two series of treatment of 10 days have been made, with a daily dose of 10 tablets. There was a week interval of rest between the two series.

"Though well tolerated, the drug had no therapeutic effect in schistosomiasis mansoni in the doses used."

[See this *Bulletin*, 1954, v. 51, 1171].

WU, Tsai-Tung, CH'EN, Teh-Huei & CHU, Ch'i. **The Relationship of Schistosomiasis to Carcinoma of Large Intestine.** *Chinese Med. J.* Peking. 1960, Mar., v. 80, No. 3, 231–42, 5 figs. [24 refs.]

The literature on this subject is first reviewed and summarized.

The average age of persons with carcinoma of the large intestine associated with schistosomiasis is 5–8 years lower than the average age of those with carcinoma of that region uncomplicated by schistosomiasis. The diseased parts of the intestine show not only the changes due to cancer but those resulting from a late stage of schistosomiasis. Some of these cases show multiple foci of cancer. Japanese workers found a higher incidence of cancer of the large intestine in areas where schistosomiasis is endemic than elsewhere.

The authors have collated further data on the subject provided by 12 pathological laboratories, 10 of which are in large cities in China where schistosomiasis is endemic and 2 in North China where this does not occur. In the endemic areas 1,193 case records were examined and, of these, 129 were found to be associated cancer and schistosomiasis. For comparison, records of 347 cases of cancer were collected from the 2 laboratories in the non-endemic areas.

Analysis of these records showed the following relevant facts.

1. The two diseases were associated in 10·8% of all cases of cancer of the large intestine in the endemic areas.
2. The age distribution of all cases of cancer of the large intestine in the endemic areas showed a preponderance in the 31–40 age-group, whereas in the non-endemic areas this was in the 41–50 age-group. By separating the 129 cases of associated cancer and schistosomiasis from the uncomplicated cases of cancer in endemic areas it was found that the age distribution in the associated cases had a much more pronounced preponderance in the 31–40 age-group and that the remainder then had a preponderance in the 41–50 age-group, giving a graphic curve similar to those cases occurring in non-endemic areas.
3. The age distribution curve of the 129 associated cases was similar in form to that of 176 cases of intestinal schistosomiasis without cancer (taken for comparison) but was an average of 5·3 years higher.
4. The ratio of males to females in uncomplicated cancer was 2:1 but in those associated with schistosomiasis was 4:1.
5. In the uncomplicated cases of cancer, 81% occurred in the rectum and recto-sigmoid and 9% in the sigmoid, descending and transverse colon. The associated group had 64% in the rectum and recto-sigmoid and 28% in the sigmoid, descending and transverse colon. It is in the inferior mesenteric veins that the heaviest infection of worms occurs in schistosomiasis.

The authors next give a brief description of the morphology of the lesions. This is based on material studied and described by Tsou and Ying (*Chinese J. Path.*, 1956, v. 2, 159) with the addition of 3 other specimens. They postulate that schistosomiasis of the large intestine leads to thickening and fibrosis of the bowel wall, to ulceration of the mucosa with areas of hyperplasia of the glandular elements which proceeds to polypoid formation. They believe that there is a relationship between the number of polyps and the extent of deposition of ova. These polyps show precancerous and cancerous changes [details not stated] and within areas of cancer they find remains of polyps which suggests to them that the malignant changes arise in the basal parts of polyps. They attribute the infrequency of metastasis to the pre-existing fibrosis in the bowel wall.

The authors conclude that their evidence indicates a true causal relationship between schistosomiasis of the large intestine and carcinoma, and that the former usually antedates the latter by 5 or more years. They think that the repeated damage and repair processes in those parts of the large intestine most affected by the ova, namely, those parts drained by the inferior mesenteric veins, leads to changes favourable to the development of cancer in certain people. *J. R. Rose*

Shen, Mai-Ling, Liang, Yu-I & Ting, Kuang-Sheng. **[Studies on Antischistosomal Drugs. XXIII. Drug Effects on Alimentary Absorption of Sb and the Promoting Effects of BAL-Glucoside]** *Acta Pharmaceutica Sinica.* 1960, Feb., v. 8, No. 2, 95–104, 1 fig. [16 refs.] [In Chinese.]

The English summary appended to the paper is as follows:—

"(1) By comparing the Sb content remaining in the alimentary tract (including feces) of mice 6 hours after intragastric administration of tartar emetic

27 mg/kg, we have studied the influences on the alimentary absorption of tartar emetic by 34 drugs consisting of surfactants, lubricants, drugs acting on nervous system, vitamins, polyalcohols, organic acids, thiols, glucose and its derivatives, etc. Only BAL-glucoside was found to be able to promote the Sb absorption.

"(2) In mice fed tartar emetic 27 mg/kg, the alimentary Sb content was 29% lower in the group with simultaneous administration of BAL-glucoside 0·21 g/kg than that in the group without BAL-glucoside. When the dosage of BAL-glucoside was increased to 2·5 g/kg, the alimentary Sb content became 60% lower.

"Mice were fed tartar emetic 55 mg/kg or fed 25 mg/kg plus BAL-glucoside 194 mg/kg daily for 14 days. The visceral Sb amounted to 128 μg/g dry weight in the former group, and 188 μg/g in the latter.

"Rabbits infected with *Schistosoma japonicum* were fed tartar emetic with BAL-glucoside (0·21 g/kg). After 24 hours, the liver Sb and the worm Sb contents were 3–4 times those in the group without BAL-glucoside.

"(3) The effect of BAL-glucoside was not due to the change of *p*H in the alimentary tract, nor simply due to the presence of SH group or glucose alone. It is surmised that, during the absorption of the glucoside residue of BAL-glucoside, the Sb was meantime conveyed in by the SH group.

"(4) BAL-glucoside enhanced the toxicity and decreased the therapeutic value of tartar emetic.

"(5) Though BAL-glucoside did not satisfy our demand, it offered a precious clue to solve the mechanism of Sb absorption and to search for ideal agents promoting the absorption of Sb."

SHIAO, Shu-Hwa, YANG, Yuan-Ching, CIE, Yu-Rai & SHANG, Yun-Cheng. **[Experimental Therapy of Schistosomiasis japonica. XII. Effectiveness of 8-Hydroxyquinoline-Antimony Complex in the Oral Treatment of Experimental Schistosomiasis in Mice]** *Acta Pharmaceutica Sinica*. 1960, May, v. 8, No. 5, 197–205, 7 figs. [In Chinese.]

The English summary appended to the paper is as follows:—

"8-Hydroxyquinoline-antimony complex synthesized in our Institute is a new antimonial compound for oral use. Its LD_{50} for mice, was 7·3–11·4 mg/20 g body weight while that of tartar emetic was 3·2–4·2 mg/20 g body weight. Even with the same process of preparation different Sb contents of 21·0, 23·1, 25·5, 43·2 and 51·3% have been obtained with differences in toxicity in increasing order. Within the limit of 21·0 to 25·5%, no difference in toxicity nor in efficacy was observed in treated animals. However, different methods of preparation resulted in significant difference in toxicity and efficacy even when the antimony contents were the same.

"When 8-hydroxyquinoline-antimony complex and tartar emetic were used at the total dosages of 1/2 or 1/3 $LD_{50} \times 14$ to treat experimentally infected mice per os in 7, 10, 14 and 20 days' courses, the efficacy of 8-hydroxyquinoline-antimony complex was superior to, but the toxicity lower than, that of tartar emetic.

"Furthermore, it was found that under the dose-schedule used, pathological lesions caused by 8-hydroxyquinoline-antimony complex were similar to those

caused by tartar emetic. They occur chiefly in the mucous membrane of the stomach and intestine, while the damage to the liver was rather slight."

MILLEMANN, R. E. & MERGENHAGEN, S. E. **Studies on the Penetration of Schistosome Cercariae. I. Action of the Antihistamine Promethazine Hydrochloride.** *J. Parasitology.* 1960, Apr., v. 46, No. 2, 155–63, 2 figs. on pl. [25 refs.]

The technique used in this work depends on the fact that if Evans blue is administered intravenously to rabbits, and cercariae are placed on the shaved skin, blue spots appear at the site of penetration, because secretions from the cercariae increase the permeability of capillaries, thus allowing the dye to escape into the subcutaneous tissues. This bluing is similar to that produced by injecting histamine or hyaluronidase subcutaneously after the administration of the dye.

Cercariae of *Schistosomatium douthitti* were used, and studies were made to see which antihistamine compounds would inhibit the reaction. The rabbits and mice used were autopsied about 12 or 8 weeks later respectively to see if the cercariae had developed into schistosomes. It was found that the subcutaneous injection of promethazine 30 minutes before the application of cercariae inhibited the Evans blue response to cercariae, to histamine and to hyaluronidase. The antihistamine (given in toxic doses) also protected rabbits and mice against infection by *Schistosoma mansoni* and *S. douthitti.*

However, these experiments do not prove that the cercariae secrete hyaluronidase, since the authors could not demonstrate this enzyme in cercariae. It is more probable that the increased capillary permeability shown by the Evans blue test is mediated through the release of histamine produced by cercarial enzymes. Promethazine antagonizes histamine and is particularly active in restoring the permeability of the capillaries. *F. Hawking*

HUNTER, G. W. **Studies on Schistosomiasis. XIII. Schistosome Dermatitis in Colorado.** *J. Parasitology.* 1960, Apr., v. 46, No. 2, 231–4. [14 refs.]

In 1956 persons bathing in Grant Lake, elevation 9,000 ft., experienced dermatitis which was suspected as being caused by schistosomes. During the summer of 1957 an investigation was made. Brevifurcate cercariae were found to be liberated by the snail *Physa propinqua*, and these were identified as *Trichobilharzia physellae*, a schistosome of mallard ducks. These cercariae were applied to the forearms of 6 volunteers. Apart from macules and papules none yielded reactions except one man who experienced slight pruritus during 24 hours. In 1958 7 cases of schistosome dermatitis occurred among bathers in Grant Lake and 4 gave a typical hypersensitive reaction to cercariae. This is the first record of schistosome dermatitis in Colorado. *F. Hawking*

DUGGAN, A. J. **The Snail Host of** *Opisthorchis felineus.* *J. Trop. Med. & Hyg.* 1960, June, v. 63, No. 6, 142–6, 3 figs. [35 refs.]

Confronted by the problem of applying the correct name to the snail intermediate host of the cat liver-fluke the author has made a very thorough

investigation of the various aspects of the situation. He reviews in detail the literature concerning the life cycle of this fluke and mentions the various names which have been used by different authors. The paper ends with a detailed review of the taxonomic position of the snail concerned and establishes that its correct name is *Bithynia leachii* (Sheppard).

C. A. Wright

AHLUWALIA, S. S. *Gastrodiscoides hominis* **(Lewis and McConnell) Leiper 1913—(the Amphistome Parasite of Man and Pig).** *Indian J. Med. Res.* 1960, May, v. 48, No. 3, 315–25, 7 text figs. & 3 figs. on pl. [22 refs.]

MONTEIRO, R. C. Tolerância e efeito de doses maciças de metoquina no tratamento da teníase. Estudo de 54 casos. **[Tolerance and Therapeutic Effect of Massive Doses of Metoquine in the Treatment of Taeniasis]** *Rev. Paulista Med.* 1957, Nov., v. 51, No. 5, 382–6. English summary (7 lines).

When working in the Health Centre of Araçatuba, Brazil, from 1953–56 the author found that a number of patients were infected with either *Taenia saginata* or *T. solium*. He therefore treated 54 patients, proved to be infected, by Metoquine [mepacrine] tablets of 0·1 gm. with dosages varying according to age. 4 tablets at 2 years of age up to 8–9 tablets for adults were given as follows: 2 tablets every 5 minutes were given to the fasting patient along with a bicarbonate solution; 3–4 hours later, a saline purgative was given. The patients' faeces were examined for at least 3 months after treatment.

36 patients were cured by this treatment; in 4 it was a complete failure. 14 patients did not return for the 3-month control examination. Side effects observed were yellow colouring of the skin in 1 patient after a second treatment 9 days after the first; nausea in 4 patients and vomiting in 19 which in some cases lasted for several hours. The author considers the treatment simple and efficacious.

[The scolex was recovered in 20 cases and in 2 the *Taenia* was eliminated but not recovered.

W. K. Dunscombe

LUBINSKY, G. **The Variability of the Number of Rostellar Hooks in Two Species of** *Echinococcus* **from North America.** *Canadian J. Zool.* 1960, June, v. 38, No. 3, 605–12, 4 figs. [14 refs.]

"Examination of six populations of *E. multilocularis sibiricensis* and nine populations of the Canadian *Echinococcus* has shown that in all of them the number of rostellar hooks was extremely variable. Over 90% of scoleces of the first species had from 20 to 32 hooks, the mode being 28. Over 90% of scoleces from the second species had from 28 to 40 hooks, the mode being 32. The difference between the populations was always statistically significant, despite a considerable overlap of the summary variation curves. Of the scoleces of the Canadian *E. granulosus*, 98·5% lie within the limits of variation pointed out by Leuckart for the European *E. granulosus*, 28 to 50 hooks."

Fochi, B. Su di un caso di echinococcosi della volta cranica. [**A Case of Echinococcosis of the Cranial Vault**] *Boll. Sanitario d. Tripolitania.* 1960, Jan.–Mar., 39–43, 4 figs. English summary (6 lines).

Juminer, B. & Zakine, J. L'hydroxynaphthoate de bephenium (Alcopar) dans le traitement de l'ankylostomose en milieu hospitalier. [**Bephenium Hydroxynaphthoate (Alcopar) in the Treatment of Hospital Patients with Ankylostomiasis**] *Arch. Inst. Pasteur de Tunis.* 1960, Mar., v. 37, No. 1, 61–80.

A comparison is recorded of the effects of Alcopar and tetrachlorethylene in the treatment of patients suffering from hookworm infection.

29 patients, 6 of whom were children, were given bephenium hydroxynaphthoate (Alcopar). Adults received 5 gm. of this product while children received one-third to one-half of the adult dose. The patients took half of the dose early in the morning while fasting, and the remaining half a few hours later. No purges were given. Stool examinations were made a week after treatment.

11 patients, 2 of whom were children, were treated with capsules of tetrachlorethylene. Adults were given one capsule (1 ml.) every 5 minutes until 6 capsules had been swallowed; while children received 2–4 capsules. The drug was not given to those under 6 years of age. The day after treatment a purge was given, and a stool examination was made a week later.

Detailed case histories of typical patients in each group are provided. An attempt was made to group the patients according to the number of worm eggs in the faeces. The conclusion reached was that Alcopar was as effective as tetrachlorethylene, was almost free from side effects, and could be used where tetrachlorethylene would be contra-indicated. *S. Bell*

Muazzam, M. G., Khaleque, K. A. & Ibrahim, M. **Hepatic Ascariasis.** *J. Trop. Med. & Hyg.* 1960, Apr., v. 63, No. 4, 95–7, 5 figs.

Migration of adult *Ascaris lumbricoides* from the intestine is not uncommon. The migration through the ampulla of Vater into the common bile duct, cystic duct, hepatic ducts and gall bladder leading to inflammation and obstruction has been recorded.

The present patient, in East Pakistan, was an ill-nourished and anaemic man of 27, with complaint of irregular fever and right upper abdominal pain, who died. During removal of the liver pus was discharged and an *Ascaris* worm emerged. The common bile duct was full of adult worms and a large number were present in the hepatic duct and one was found in the gall bladder. In culture of the pus *Pseudomonas pyocyanea* was obtained. Sections of the walls of cystic areas containing *Ascaris* showed a number of chronic inflammatory cells, plenty of fibroblasts and slight fibrosis with necrosed liver cells. Ova were found in various parts of the liver. There were large numbers of *Ascaris* in the intestine and a few in the oesophagus.

The name of hepatic ascariasis is proposed to describe the entity which has been outlined.

[This paper is illustrated with 3 photographs and 5 photomicrographs.]

Philip Manson-Bahr

ORAM, R. H. **Filariasis on the North Nyasa Lake Shore (II).** *Central African J. of Med.* 1960, Apr., v. 6, No. 4, 144–5, 2 figs.

In August and September 1957 3 villages were surveyed on the north shore of Lake Nyasa for filariasis in an area known to be infected with *Wuchereria bancrofti* [this *Bulletin*, 1958, v. 55, 1146]. They are situated on the south bank of the Songwe river which constitutes the boundary between Nyasaland and Tanganyika.

Blood films were taken between 9.30 p.m. and 2 a.m. and about half the total number of villagers were examined. The figures obtained showed a steady rise in the percentage of inhabitants with microfilaraemia until the age of 30 and thereafter the percentage remained constant. The maximum was reached a little earlier in men than in women. There were not sufficient villagers in the over 60 age-group for the figure to be of value.

The clinical signs of filariasis included elephantiasis of the legs, penis and scrotum, hydroceles and gross enlargement of the inguinal glands. The graph showed a steady increase in these when adult life had been reached. The maximal microfilaraemia was 44% in males of the 21–30 age-group.

Philip Manson-Bahr

LEBIED, B. Mise au point à propos d'une nouvelle méthode de dissection des vecteurs des filarioses. Le but de cette méthode. [**Rectification on a New Method of Dissection of Vectors of Filariasis. The Scope of this Method**] *Riv. di Parassit.* Rome. 1960, Mar., v. 21, No. 1, 71–9, 4 figs. [11 refs.]

This is mainly a plea for recognition of the method described by the author [this *Bulletin*, 1952, v. 49, 789] for staining filariae *in situ* in the insect vector. A modification of this method has been described, with suitable acknowledgments to the original method, by NELSON [*ibid.*, 1958, v. 55, 1360].

A method is described here for preparing permanent preparations of filariae in insect tissue. The paper is illustrated by poorly reproduced photographs which certainly do not do justice to the author's claim that the method described makes possible the examination of the anatomical and physiological relationship between the filarial larvae and the cells of the arthropod host. [From the abstracter's experience of these staining methods for filariae in the insect, this claim may well prove to be justified.]

B. R. Laurence

MARCH, H. N., LAIGRET, J., KESSEL, J. F. & BAMBRIDGE, B. **Reduction in the Prevalence of Clinical Filariasis in Tahiti following Adoption of a Control Program.** *Amer. J. Trop. Med. & Hyg.* 1960, Mar., v. 9, No. 2, 180–84, 2 figs.

BEYE and his colleagues [this *Bulletin*, 1953, v. 50, 47] assessed the prevalence in males of non-periodic filariasis in Tahiti, prior to the institution of a control programme. Elephantiasis and microfilarial prevalence were recorded in regular clinical and blood surveys which included 3,390 males in 15 rural districts of Tahiti. In addition, 7 widely distributed areas in the island were set apart for epidemiological studies. In these data information concerning 203

males examined for clinical manifestations other than elephantiasis has been included.

In 1954 these districts were taken over in the control programme instituted by KESSEL [*ibid.*, 1958, v. 55, 194]. It had 2 main objects: (1) mass treatment of the population with diethylcarbamazine and (2) mosquito-control by the elimination of mosquito breeding places within 100 metres of each dwelling. The mass treatment programme consisted of an initial course of 12 monthly doses of 6 mgm. per kgm. of body weight of diethylcarbamazine.

It was considered that data collected by physical examination of the male population for clinical signs and symptoms of filariasis and blood surveys 10 years after the first survey and 5 years after incorporation of districts and areas into standardized island-wide filariasis control programmes, would provide some significant data for comparing prevalence rates before and after control.

In the surveys within the 7 small areas, a history of lymphangitis, enlarged epitrochlear, femoral and inguinal lymph glands, the presence of hydroceles and additional signs other than elephantiasis were considered. In persons over the age of 20 the percentage of those free from signs of clinical filariasis increased from 16% in 1949 to 49% in 1959.

Also, in the island of Moorea, where the programme was inaugurated in 1956, a similar trend in the reduction of microfilaraemia and clinical symptoms was noted. As no new cases have appeared, it follows that when the present subjects die, elephantiasis must cease to exist in those islands where an adequate control has been established.

During mass treatment with diethylcarbamazine of Tahitians certain observations of value have come to light. Thus, persons in lymphangitic attack have requested medication voluntarily because they have heard from their friends that taking diethylcarbamazine prevented further attacks; others, who at first hesitated about accepting medication for filariasis, willingly swallowed the dose when they had observed its anthelmintic effect on their own and neighbour's children by finding dead ascarids in their faeces.

Although some workers, notably IYENGAR, advocate mosquito control by itself for the eradication of filariasis, the very marked reduction in the clinical manifestations with combined drug and vector control has demonstrated that the combination gives rapid progress and practical results.

The final results were as follows:— overall microfilaraemia was reduced from 37% to 6·5%; elephantiasis dropped from 6·9% to 2·2% for all males, while in the significant 20–40 year age-group it was reduced from 5% to 0·6%; total hydroceles were reduced from 9·8% to 3·2%; acute filarial lymphangitis fell from 36% to 4% in males over the age of 20; no fresh cases of elephantiasis or hydroceles developed after the application of control measures.

Philip Manson-Bahr

LAING, A. B. G., EDESON, J. F. B. & WHARTON, R. H. **Studies on Filariasis in Malaya: The Vertebrate Hosts of *Brugia malayi* and *B. pahangi*.** *Ann. Trop. Med. & Parasit.* 1960, Apr., v. 54, No. 1, 92–9, 6 figs. on 2 pls. [18 refs.]

Blood surveys of wild and domestic animals carried out in East Pahang, Malaya, in order to define the animal reservoirs of *Brugia malayi* and *B. pahangi*, showed that *B. malayi* occurred naturally in the dusky leaf-monkey

(*Presbytis obscurus*) (19 infected out of 25), in the domestic cat (9 out of 88), the common palm-civet (1 out of 44), the long-tailed macaque monkey (4 out of 116), the wild cat (*Felis bengalensis*) (1 out of 7), and the pangolin (*Manis javanica*) (2 out of 11).

B. pahangi occurred naturally in the domestic cat (18 out of 88), the dog (5 out of 25), the slow loris (*Nycticebus coucang*) (8 out of 25), the palm-civet (*Paradoxurus hermaphroditus*) (12 out of 44), as well as in a wild cat, pangolin, moon-rat and giant squirrel.

"The very high infection rate of 76 per cent. in leaf-monkeys suggests that these animals form a reservoir of the infection which will impede attempts to control the human disease. Wharton *et al.* [see this *Bulletin*, 1958, v. 55, 1261] found that in a small population the microfilaria rate, which had been reduced from 49 per cent. to 10 per cent. after mass treatment, rose steadily over the subsequent three years to 22 per cent. They considered that many of the re-infections had come from an animal reservoir, since the infectivity of the population to mosquitoes had been reduced by 99 per cent. Cats living in close association with man are also infected, but *B. pahang*i (21 per cent.) is more common among naturally infected cats than *B. malayi* (11 per cent.). These cat infections are probably of little importance to man, since mosquito hosts are known to feed more on man than on cats (Edeson and Wharton, 1958b), and man is more likely to be a reservoir for the cats than vice versa.

"The many hosts of *B. pahangi* make up a very considerable reservoir of infection, to which man living in this endemic area is also exposed, and the successful transmission of *B. pahangi* from a civet (*P. hermaphroditus*) to man, with the production of clinical filariasis and microfilaraemia (Edeson, Wilson *et al.*, 1960), has given a new significance to this parasite. *B. malayi* is undoubtedly the dominant human parasite, but *B. pahangi* may occasionally produce an infection in man, and it is impossible to say what part the parasite may play in the production of clinical symptoms." *W. E. Kershaw*

TAYLOR, Angela E. R. **Maintenance of Filarial Worms** *in vitro*. *Exper. Parasit.* New York. 1960, Apr., v. 9, No. 2, 113–20, 3 figs. on pl. & 2 text figs.

Attempts were made to cultivate different stages of filarial worms *in vitro*. Microfilariae remained alive at 22°C. in various media for 10–14 days. After 10 days microfilariae of *Loa loa* showed division of the G cells 1 and 2 but otherwise there was no development. Various mosquito stages of *Dirofilaria immitis* were maintained at 22°C. for 3–13 days but apart from moulting no further growth or development occurred. Infective larvae survived quite well and moulted but did not increase significantly in size. The adult worms of *Litomosoides carinii* survived *in vitro* for 23 days at 37°C.; and for 18 days the females continued to produce microfilariae, which is a sign of a healthy physiological state. For the first 10 days each female worm produced approximately 10–15 thousand microfilariae per day. The best medium consisted of fresh rat serum plus 199 solution. *F. Hawking.*

See also p. 1115, D'HAUSSY & UEMURA, A propos de l'origine génétique des lésions choriorétiniennes observées chez les onchocerquiens. [**Concerning the Genetic Origin of Chorioretinal Lesions in Patients with Onchocerciasis**]

Cloetens, W., De Mey, D., Mahieux, A. & Solomentsev, D. Cardiopathie filarienne. [**Filarial Cardiopathy**] *Ann. Soc. Belge de Méd. Trop.* 1959, Dec. 31, v. 39, No. 6, 799–816, 12 figs. [27 refs.]

This report concerns a 28-year-old man who had lived for 10 years in the Belgian Congo. He first became ill in October 1956, and a detailed description of the course of his illness indicates that he developed heart failure. The cause of this was obscure. However, there was eosinophilia and a nodule, believed to be due to onchocerciasis, was found in the left iliac crest. The authors believe that this was a case of endomyocardial fibrosis, the cause of which they postulate as filariasis. [They are too ready to assume, however, that residence in an endemic area of various types of filariasis necessarily means that a person is infected with these. Furthermore, an association in time between the discovery of a filarial infection and the appearance of heart failure cannot be taken as good evidence of cause and effect.] *S. Bell*

Friedheim, E. A. H. & De Jongh, R. T. Deux observations d'effets thérapeutiques dans l'onchocercose après des traitements au Mel W (pentylthiarsaphénylmélamine) et au TWSb (dimercaptosuccinate d'antimoine). [**Two Observations of Therapeutic Results in Onchocerciasis after Treatment with Mel W (Pentylthiarsaphenylmelamine) and with TWSb (Dimercapto Succinate of Antimony)**] *Bull. Soc. Path. Exot.* 1960, Jan.–Feb., v. 53, No. 1, 43–6.

These observations were made in Liberia on 2 patients each with sleeping sickness and onchocerciasis, treated with Mel W and (in one case) with TWSb also. Progress was followed by means of multiple skin snips.

The first patient was a woman aged 28, weighing 45 kgm. with two small nodules in the pelvic region. She was given 2 series of 4 daily intramuscular injections of Mel W of 120 or 200 mgm. each with an interval of 17 days between. One and a half months later the number of microfilariae was unchanged but a year later they had become rare. The nodules had disappeared by the last examination.

The second patient was a woman of 25 years and 45 kgm., who showed several nodules in the pelvic region and moderate skin changes (atrophy, hyperkeratosis, ichthyosis etc.). Her treatment consisted of 4 daily intramuscular injections of Mel W of 150 or 200 mgm. After 53 days she also received 5 daily intramuscular injections of 400 mgm. TWSb. Up to the fifth month from the first treatment the skin condition was unchanged, but from the sixth to eleventh month it improved greatly. By the thirteenth month the hyperkeratosis had practically disappeared and the iliac nodules were no longer palpable. At the ninth, tenth and eleventh months no microfilariae were found in the skin snips although initially they had been numerous. It is noteworthy that the full effects of these short courses of treatment were not manifested until 9 months or more later. *F. Hawking*

Crosskey, R. W. **Aspects of Black-Fly Control and Entomology in the New World in relation to the *Simulium* Problem in Nigeria.** *Bull. World Health Organization.* Geneva. 1959, v. 21, No. 6, 727–36. [17 refs.]

Active control programmes aimed at control rather than total eradication of the blackfly, *Simulium*, exist in Canada, U.S.A. and Mexico in the New World and northern Nigeria in the Old World. In Canada and the U.S.A. the object of control is to reduce the mass biting nuisance, whereas in Mexico and northern Nigeria, it is to assist in breaking the transmission cycle of onchocerciasis.

The usual method of control is the application of larvicides to rivers and streams where the flies breed. However, the topography of the different control areas makes it impossible to have uniform techniques in control. For example, in the Canadian control area the multiplicity of streams, dense undergrowths and the lack of roads and trails make larviciding from the ground almost impossible and have forced the adoption of air spraying techniques. In the Mexican control area, on the other hand, the mountainous terrain clothed with tropical forests, which often conceal the breeding streams, makes aerial larviciding impossible and ineffective. The requirements for blackfly control are very different in Nigeria, where the species concerned, *Simulium damnosum*, breeds in large rivers, easily accessible from the ground.

In Canada and the U.S.A., successful control of the blackflies is, in large measure, due to extensive biological studies which have been carried out. This is in contrast to the situation in Nigeria, where blackfly control to alleviate the distress of onchocerciasis has, to some extent, gone on in the absence of any intensive preliminary or concurrent biological study of the insect. This has resulted in considerable lacunae in our knowledge of these flies which, according to the author, may well prove the loopholes through which the flies could evade control.

The author concludes with some comments on the entomological aspects of onchocerciasis in the New World and the Old. In Mexico and Guatemala the disease occurs in closely circumscribed zones, between 450 metres and 1,500 metres above sea level, and is associated with coffee growing areas, although the vectors, *Simulium ochraceum*, *S. metallicum* and *S. callidum*, have a much more extensive distribution. In Nigeria the onchocerciasis areas are diffuse, are not dependent on altitude or associated with any particular ecological situations and the distribution of the vector, *S. damnosum*, closely parallels the distribution of the disease. A point of considerable interest, not easy to explain, is the low infection rate of *Onchocerca volvulus*, 1%, in the New World vectors [this *Bulletin*, 1956, v. 53, 518] as compared with rates of 5% to 20% in the Old World vectors [*ibid.*, 1955, v. 52, 68]. Important differences exist between the New World and Old World vectors in their seasonal population fluctuations, breeding and biting habits. The Mexican and Guatemalan vectors usually bite around the neck, shoulders and head while the African vector bites almost entirely on the legs—preferences which appear to be correlated with differences in skin sites with the heaviest microfilarial densities.

M. G. R. Varma

BOURREL, P. Gangrène du scrotum par élimination massive de filaires de Médine. [**Gangrene of the Scrotum from Massive Discharge of** *Dracunculus medinensis*] *Méd. Trop.* Marseilles. 1960, May–June, v. 20, No. 3, 382–3, 1 fig.

Report of a case.

Olson, L. J., Richards, B. & Ewert, A. **Detection of Metabolic Antigens from Nematode Larvae by a Microculture-Agar Gel Technique.** *Texas Reports on Biol. & Med.* 1960, v. 18, No. 2, 254–9, 3 figs. [9 refs.]

A new micro-technique is described for diffusion in agar gel so as to obtain bands of precipitation formed by antigen and antibody. This has been applied to living larvae of *Trichinella spiralis* obtained from the muscles of rats. Judging by the lines produced by living larvae, by the secretions of larvae, and by disintegrated larvae, it seems that the larvae, while living in the host, liberate 3 to 5 metabolic antigens and that 9 others are liberated when the larvae die and disintegrate.

[This is an interesting technique, which should be studied in the original by those interested.] *F. Hawking*

DEFICIENCY DISEASES

McLaren, D. S. **The Pattern of Early Growth in Sukumaland, Tanganyika.** *J. Pediatrics.* St. Louis. 1960, June, v. 56, No. 6, 803–13, 7 figs. [16 refs.]

This paper shows that in Sukumaland, Tanganyika, infant growth pattern is similar to that found in surveys elsewhere. Until the age of 6 months growth curves are similar to those in Europe and North America, but after the weaning process begins African children fall behind those of advanced countries, and never catch up again. Observations were made at a town clinic in Mwanza and a rural clinic; growth of children attending the Mwanza clinic was almost identical with that found at Kampala, Uganda [this *Bulletin*, 1956, v. 53, 478], and compared favourably with that of the rural children. Yet overt kwashiorkor is commoner at Kampala. It appears that dietary balance as well as dietary deficiencies are important factors in its development.

If the child's diet was satisfactory, sudden loss of weight due to infections was rapidly regained, and the rate of growth was not affected. The records of 8 babies with exceptional weights, over 24 pounds, at 1 year were analysed. All had been heavier than average at 1 month but they did not necessarily have high birth weights. 6 of the 8 had almost no illness during their first year. Several growth curves are given. The main table gives mean weights and weight increments for different weight groups at 1 month of age.

B. B. Waddy

Gopalan, C. **Diseases of Nutritional Deficiency of Children in South India. A Review of some Salient Conditions.** *J. Pediatrics.* St. Louis. 1960, July, v. 57, No. 1, 89–100. [40 refs.]

McKay, S. R. **Growth and Nutrition of Infants in the Western Highlands of New Guinea.** *Med. J. Australia.* 1960, Mar. 19, v. 1, No. 12, 452–9, 8 figs.

This paper describes the conditions of infants in a small area of the Western Highlands of New Guinea, where the medical services are provided by a Baptist Mission. The main articles of diet are sweet potato, banana and sugar cane. Protein intake is low and kwashiorkor is common and often severe. The need for additional foods rich in protein is stressed. *R. Passmore*

Suarez, R. M. **Nutritional Problems in Puerto Rico, 1930–1958.** *Bol. Asoc. Med. de Puerto Rico.* 1960, Mar., v. 52, No. 3, 79–88. [14 refs.]

In 1930 hookworm or iron deficiency anaemia, sprue, oedema due to hypoproteinaemia and pellagra were rampant in Puerto Rico. Beriberi, scurvy and other deficiency states were often seen. The crude death rate was about 20 per 1000. Now nutritional disorders are rarely seen and the death rate is 7. Net income per head (now $443) has risen nearly four-fold, annual consumption of milk and milk products (now 400 lb per year) has also risen nearly four-fold. There is a greatly increased consumption of meat and fresh vegetables. Physicians now number one per 1,389 of population, a three-fold increase.

This paper records, with a wealth of statistical detail and much sensible comment, the transition of the island from a rural slum to a relatively prosperous community, although conditions are still far from ideal. *R. Passmore*

Zubiran, S., Martinez, P. D., Balam, G. & Chavez, A. Estudio epidemiologico de la desnutrición en México. **[Epidemiological Study of Malnutrition in Mexico]** *Salud Pública México.* 1960, Jan.–Mar., v. 2, No. 1, 111–18, 4 graphs.

This paper is from the National Institute of Nutrition of Mexico which has developed out of the Hospital for Diseases of Nutrition. It houses also the Central Office for National Nutrition. The last-named has investigated the medico-social aspects of nutrition throughout the country.

A close study has recently been made of the diet and the nutritional state of 11 rural and suburban communities: they were places with average vital statistics and average fertility of the soil. The features studied were economic, social, cultural and sanitary together with the incidence of nutritional diseases such as goitre, pellagra, and diabetes. In each of the communities an intensive study, clinically and in the laboratory, was made of 20 to 50 families.

The communities studied were essentially agricultural: 90% of the families owned the property where they lived but only 10% produced their own food. Weaning of infants is late, generally in the second year. By that time the child is already malnourished and until the age of 4 years his food is determined by many taboos and prejudices. The diet is deficient in first class protein such as meat and milk and the child is prone to have diarrhoea and fevers.

The main food is maize which provides 75% of the calories and 50% of the proteins. The maize is supplemented by small amounts of kidney beans, meat,

green vegetables, wheat, fruit, milk and eggs. The deficiencies in the diet are vitamins A, C and riboflavin together with calcium and amino acids.

The children are stunted and present signs of dietary deficiency in the conjunctivae, the skin and the mucous membranes. Some develop pellagra and their resistance to most diseases is lowered.

The investigation has shown that if the diet contains even 15 gm. of animal protein per person per day the growth of the children will be normal and the pre-school mortality will be below 20 per 1,000, but in the ill-nourished communities more than 5% of the children show signs of malnutrition and the pre-school mortality exceeds 40 per 1,000.

The facts having been revealed, an educational campaign is needed to promote the inclusion in the diet of more animal protein, more fruit and more green vegetables. This education should be given at Maternal and Child Welfare Centres where special attention should be given to the age-group 1–4. The necessary food can be produced locally without great cost or special staff. Better diet is essential for an improvement in the public health.

[The charts are clear and in considerable detail but the text is in very general terms.] *Allen Daley*

FLORES, Marina; GARCÍA, Berta; BÉHAR, M.; ARROYAVE, G.; SCRIMSHAW, N. S. **The Nutritional Status of Children of Pre-School Age in the Guatemalan Community of Amatitlán. 1. Comparison of Family and Child Diets** [FLORES & GARCÍA]. *Brit. J. Nutrition*. 1960, v. 14, No. 2, 207–15. [11 refs.] **2. Comparison of Dietary, Clinical and Biochemical Findings** [BÉHAR, ARROYAVE, FLORES & SCRIMSHAW]. *Ibid.*, 217–30, 2 figs. [32 refs.]

The studies were made in a poor agricultural community of mixed Mayan Indian and Spanish stock. A monthly income equivalent to 10 U.S. dollars per person was taken as the lower limit consistent with minimum nutritional and health standards. From 40 families below this limit Flores and García, in the first study, selected 20 boys and 20 girls under 5 years of age and compared their diets with those of their families. In the second, Béhar *et al.* examined these 40 children, whose dietary history was obtained, for clinical and biochemical evidence of malnutrition, and obtained clinical and biochemical data only for an additional sample of 37 children under 7 years of age.

The nutritive value of diets was calculated with food composition tables, with some analyses, and the amounts of each nutrient estimated compared with allowances recommended by INCAP (*Instituto de Nutrición de Centro América y Panamá*) based on the U.S.A. National Research Council's allowances. The total daily intakes of 32 families were also measured, the nutrient content being calculated in the same way, and compared with estimated needs calculated for each family. Flores and García found that by these standards the dietary intake of most children was inadequate, especially of vitamin A, riboflavin, calcium, ascorbic acid and protein of good quality. The most marked deficiencies occurred between 1 and 2 years of age, and the children's diets compared poorly with those of their families, although family diets were themselves inadequate. The money spent on food was insufficient for the whole family and

the amount spent on feeding the young child was disproportionately small. Full details of the diets, and their nutritive value are given in the paper. The authors note that very few of the many reports of family food consumption investigate the distribution among family members, and their paper confirms a suggestion that calculation of dietary adequacy without this can be misleading.

Béhar *et al.* give a table of ages, heights, weights and mean daily intake of nutrients for each of 32 of the children whose diets were investigated in the previous paper. In addition to the dietary defects noted there, they note that 18 of them received less than 5 gm. of animal protein, and fat intake was low. Clinical examinations showed that, plotted against curves of reference for height, weight, and age adopted by INCAP for well nourished children, nearly all fell below the sixteenth percentile in weight and more than one standard deviation below the mean in height, though height/weight ratio was frequently normal; that measurements of skinfold thickness were very low; that alterations in texture, implantation, and pigmentation of hair, follicular keratosis, goitre and *Ascaris lumbricoides* infections were common; and that 28 of 75 children had dental caries, and 31 had eroded enamel across the base of the incisors. 5 children had serum protein levels below 6 gm./100 ml. and about the same numbers low serum cholinesterase and alkaline phosphatase; there was a positive correlation between serum protein and alkaline phosphatase, but not with cholinesterase. Half the children had serum-vitamin A levels below 20 μgm./100 ml. with generally low serum-carotene particularly in the younger children; and serum levels of riboflavin, both as free plus flavin mononucleotide (FMN) and as flavin adenine denucleotide (FAD) suggested a relative deficiency of riboflavin.

It is concluded that the dietary evidence of insufficient calories and protein fully accounts for the degree of retardation of growth observed. The intakes of vitamin A and riboflavin would be expected to be limiting, and the biochemical evidence is compatible with the low intake. The lack of more noticeable signs of deficiency of these two vitamins may have been due to decreased requirement because of the decreased body mass caused by growth failure. Protein deficiency was shown also by the frequency of hair changes of the type found in kwashiorkor as well as by the biochemical findings. A few children were on the borderline of severe protein deficiency. Though the observed intake of ascorbic acid was low, there was neither biochemical nor clinical evidence of ascorbic acid deficiency, and this suggests that dietary observation was incomplete, as sources of ascorbic acid are consumed by the children between meals.

The three types of findings, clinical, biochemical, and dietary, served to complement one another and made possible an evaluation of the nutritional status which could not have been achieved without all three. *T. P. Eddy*

BARON, D. N. **Serum Transaminases and Isocitric Dehydrogenase in Kwashiorkor.** *J. Clin. Path.* 1960, May, v. 13, No. 3, 252–5, 1 fig. [21 refs.]

This is an excursion into what might be called racial biochemistry. Three serum enzymes, serum glutamic oxalacetic transaminase (SG-OT), serum glutamic pyruvic transaminase (SG-PT), and serum isocitric dehydrogenase (SI-CD), were determined in 6 groups of subjects. These were:

(1) 22 normal Europeans who were studied at the Royal Free Hospital in London.
(2) 14 healthy Nigerian medical students aged from 20 to 30 who were eating a mixed diet containing about 70 gm. protein daily. These and the following groups were all seen at the University College Hospital, Ibadan, Nigeria.
(3) Undernourished persons from an agricultural village about 10 miles from Ibadan; they included 7 adults whose daily protein intake was about 40 gm. and 10 children whose protein intake was not known but was probably less.
(4) 11 children seen at the Ibadan Hospital who were suffering from protein undernutrition (kwashiorkor). They were aged from 1 to 6 years.
(5) 9 such children who had recovered from this condition.

The range of all three enzymes, particularly of the SG-OT, was slightly lower in the normal Nigerian than in the normal European. All three enzymes were considerably raised in florid malnutrition and there was also a slight rise in undernutrition. The SG-PT was in all cases less affected than the two other enzymes. The increased serum enzyme activity in undernutrition is thought to be due to the effect of tissue wasting on the liver and also on voluntary muscle.

H. Lehmann

MONTGOMERY, R. D. **Magnesium Metabolism in Infantile Protein Malnutrition.** *Lancet*. 1960, July 9, 74–6, 1 fig. [18 refs.]

Evidence is presented showing that there is depletion of the tissues of magnesium in kwashiorkor. Analyses of magnesium content were carried out by flame spectrophotometry. In 12 Jamaican infants with kwashiorkor, muscle biopsy was carried out soon after admission and 5–9 weeks later. The mean magnesium and potassium contents rose from 10·1 and 56 respectively to 13·9 and 70 mEq. per kgm. of wet muscle. In 27 infants, the mean magnesium level in the red cells rose on treatment from 3·80 to 4·05 mEq. per litre. The serum level (1·73) remained unchanged. Urinary excretion of magnesium was under 0·2 mEq./day at the start of treatment, which is very low. After 40 days it had risen to 0·8 mEq./day.

[See also this *Bulletin*, 1958, v. 55, 563.] *R. Passmore*

EL GHOLMY, A., EL NABAWY, M., SHUKRY, A. S., ISMAIL, Soraya & EL HAWARY M. F. **Biochemical Studies on Serum Proteins in Kwashiorkor of Egyptian Infants.** *J. Trop. Med. & Hyg.* 1960, June, v. 63, No. 6, 137–41, 4 figs. [16 refs.]

The serum proteins were studied in 47 children with kwashiorkor in Cairo by electrophoretic methods. Levels of albumin and alpha 1, alpha 2, beta and gamma globulins were all found to be reduced, but most markedly the albumin. After treatment levels returned to almost normal.

[See also this *Bulletin*, 1960, v. 57, 512, 837.] *R. Passmore*

CRAVIOTO, J., GOMEZ, F., RAMOS-GALVAN, R., FRENK, S., MONTAÑO, Evangelina L. & GARCIA, Nelly. Metabolismo proteico en la desnutrición avanzada: concentración de aminoácidos libres en el plasma sanguíneo. **[Protein Metabolism in Advanced Malnutrition—Concentration of Free Amino Acids in the Plasma]** *Bol. Oficina Sanitaria Panamericana.* 1960, May, v. 48, No. 5, 383–91, 1 fig. [25 refs.]

When 13 children with advanced malnutrition were examined, it was noted that all 7 of those who were oedematous and had skin lesions had a serum albumin below 2 gm.%, whereas all the 4 infants of the non-oedematous group in which this estimation was done had a serum albumin above 2·5 gm.%. The concentration of free amino acids in the plasma was determined by chromotography. It was universally lower than in normal children. There was a good deal of variation but arginine, leucine and valine were universally low in all 13 sera. *H. Lehmann*

WATERLOW, J. C.; WILLS, Verity G.; GYÖRGY, P. **Balance Studies in Malnourished Jamaican Infants. 1. Absorption and Retention of Nitrogen and Phosphorus** [WATERLOW & WILLS]. *Brit. J. Nutrition.* 1960, v. 14, No. 2, 183–98, 5 figs. [47 refs.] **2. Comparison of Absorption and Retention of Nitrogen and Phosphorus from Human Milk and a Cow's-Milk Mixture** [WATERLOW, WILLS & GYÖRGY]. *Ibid.*, 199–205. [10 refs.]

i. The paper records balance studies made on 37 babies in various stages of kwashiorkor. The absorption of dietary nitrogen was always more than 90% (after allowing for faecal metabolic nitrogen): similarly, nitrogen retention was high, more than 50% of the absorption, except when intakes above 0·5 gm./kgm. of body weight were given. The data indicate that a minimum of 96 mgm. nitrogen/kgm./day, equivalent to 0·6 gm. protein/kgm./day is necessary to secure nitrogen balance. 5 of the babies were unable to respond to treatment and died. Yet, in all, absorption and retention of nitrogen was satisfactory and they were in positive nitrogen balance. It is concluded that death was not due to irreversible failure of nitrogen utilization.

In general more phosphorus was retained in relation to nitrogen than would be expected from the ratio of the elements in normal muscle. This extra phosphorus may be taken up by bone.

ii. In 17 of the babies, described in the previous paper, it was possible to make a direct comparison between human milk (obtained from a milk bank) and a cow's milk mixture. Nitrogen absorption was excellent with both, but retention when on human milk (49%) was higher than when on cow's milk (41%). This difference is small, but might be of biological significance to infants living on marginal amounts of protein.

On both types of milk 70% of ingested phosphorus was absorbed. As human milk contains only half as much phosphorus as cow's milk, the babies on the latter were absorbing more. The absolute amounts of phosphorus retained by the tissues were approximately the same for the two milks.

R. Passmore

UDANI, P. M. **Neurological Manifestations in Kwashiorkor.** *Indian J. Child Health.* 1960, Feb., v. 9, No. 2, 103–12, 3 figs. [14 refs.]

This paper records a study of mental and nervous changes in children in Bombay suffering from kwashiorkor. 15 patients of ages ranging from 6 months to 4 years showed changes considered typical of kwashiorkor: oedema, dermatitis, stunting of growth, mild anaemia and lowered plasma albumin levels.

Misery and irritability were common, associated in the majority with periods of apathy and drowsiness. 2 patients having these changes became comatose and died, and at post-mortem examination marked fatty changes were found in their livers. In one case convulsions had preceded death, and these were believed to be due to hypoglycaemia. In the older children in this series apathy was a very marked feature, and in 2 children biting and hair-pulling were especially noted. The children all showed weakness of voluntary muscles with hypotonia. There was loss of the knee jerks, followed later in some by loss of the ankle jerks. No sensory changes were detected. Recovery of tendon reflexes occurred from 15 days to 6 weeks after treatment. In 2 patients there was upper motor neurone disorder with extensor plantar responses, exaggerated tendon reflexes and ankle clonus. One child recovered fully after a high protein diet had been given for 4 weeks.

During treatment for kwashiorkor, which included treatment of secondary or associated infections, high protein diet, multi-vitamin preparations, and in some cases blood transfusion, 3 patients showed coarse intention tremor affecting the hands and arms. Trial was made with Parpanit (caramiphen hydrochloride) to control the tremor.

Discussion of the aetiology of these lesions leads to no conclusion except that in grave malnutrition there must be disturbed metabolism of the central nervous system. *S. Bell*

PURSHOWTHAM RAO, G. **Clinical Features of Kwashiorkor in Hyderabad.** *Indian J. Child Health.* 1960, Apr., v. 9, No. 4, 198–206, 12 figs.

The clinical features of 38 patients admitted to hospital are clearly and fully described: they conform with descriptions of the disease in other parts of the world. However, a microcytic anaemia was frequently present and in some children was severe. The bone marrow when examined was normoblastic and hyperplastic. Only one child carried hookworms and the cause of the anaemia was not clear. Less than half the children were infected with *Ascaris*.

R. Passmore

PURSHOWTHAM RAO, G. **Treatment of Kwashiorkor with Vegetable Protein Diets.** *Indian J. Child Health.* 1960, Apr., v. 9, No. 4, 207–13.

A clinical trial is reported on 21 of the patients described in the previous paper. One group received skimmed milk, another a Multipurpose Food and a third the Multipurpose Food plus an injection of 50μgm. of vitamin B12 on alternate days. The Multipurpose Food was provided by the Central Food Technological Research Institute, Mysore, and prepared from defatted groundnut flour

and Bengal gram flour. It contained no protein of animal origin. Most of the children did well in all three groups. Judged by clinical criteria (the time taken for oedema to disappear, gain in weight, rise in serum albumin) there was no difference between the three groups. This is an important demonstration of the fact that kwashiorkor can be effectively treated without animal protein.

It is pointed out that the preparation of Multipurpose Food at the village or town level is not difficult. It should be most valuable in the prevention of kwashiorkor. *R. Passmore*

DEAN, R. F. A. **Treatment of Kwashiorkor with Moderate Amounts of Protein.** *J. Pediatrics*. St. Louis. 1960, May, v. 56, No. 5, 675–89, 1 fig. [18 refs.]

This paper reports a therapeutic trial in Kampala, Uganda, in which the effects of two types of biscuits were compared with the effect of milk protein. The biscuits were made of mixture of peanut, maize and wheat flours; one type contained a moderate amount of dried skimmed milk and the other only a small quantity. In all the diets protein provided about 17% of the calories. Clinical assessment was made on changes in weight, serum protein levels and levels of serum amylase and cholinesterase. The milk diet and the biscuit containing moderate amounts of added milk gave satisfactory results, but improvement was much less rapid with the biscuits containing little milk.

This paper contains a useful discussion of methods of grading the severity of the disease and assessing progress. *R. Passmore*

ARÉTAS, R. E. Effet d'une supplémentation protidique contrôlée sur une population infantile. [**The Effect of a Controlled Supplement of Protein on a Child Population**] *Soc. Méd. Afrique Noire Langue Française*. Dakar. 1959, v. 4, No. 4, 400–405, 1 chart.

Biscuits enriched with fish protein were distributed to children aged 2-11 years in two villages near Dakar from October 1957 to October 1958. The children in these two villages gained more weight than the children in a nearby village not receiving the biscuits. The biscuits proved to be readily acceptable to the children. *R. Passmore*

PAYET, M., SANKALÉ, M., ARMENGAUD, M., FERNEX, M., BOURGEADE, A. & CACHIA, P. Le béribéri endémique du Casamançais transplanté à Dakar. [**Endemic Beriberi in Casamance People who have migrated to Dakar**] *Bull. Soc. Méd. Afrique Noire Langue Française*. Dakar. 1960, v. 5, No. 1, 23–38. [19 refs.]

Beriberi arises in the people from Lower Casamance who migrate to Dakar. They retain their rice-eating habits, but the rice available in the town is usually machine-milled. Less fruits and pulses are available than in their old homes, but intake of alcohol is sometimes greatly increased.

The case histories of 16 patients (12 men and 4 women) are recorded in full. Usually both the cardiovascular and neurological features of the disease are present and the mixed type of beriberi is common. The patients all responded in a spectacular way to vitamin B1 therapy.

This interesting paper is a useful reminder that the classical deficiency diseases are by no means extinct. The authors conclude with a discussion of the social and economic problems of the migrants and state the need for health education among the urbanized Casamancans. *R. Passmore*

WOLF, P. L. & LEVIN, M. B. **Shöshin Beriberi.** *New England J. of Med.* 1960, June 30, v. 262, No. 26, 1302–6, 8 figs. [21 refs.]

"Two cases of Shöshin beriberi, which is acute, fulminant cardiac beriberi, a disease in which the integrity of the cardiovascular system is severely affected by thiamine deficiency, are reported, along with the autopsy findings in 1 case. This disease is a medical emergency that has not received sufficient emphasis in the American medical literature."

[See this *Bulletin*, 1946, v. 43, 945.]

ŠALAMON, T., JEFTIC, Z. & KARAMEHMEDÖVIC, R. Dalji prilog ispitivanju pelagre u Bosanskoj Krajini. [**Study of Pellagra in the Province of Bosanska Krajina, Yugoslavia**] *Acta Med. Iugoslavica.* 1960, v. 14, No. 1, 20–27. [15 refs.] French summary.

In this community pellagra is endemic. The authors examined 1,043 members of the population and found the following morbid conditions:

Pellagra	55 cases
Diffuse melanosis of the exposed skin	24 „
Common pigmentation of the exposed skin	336 „
Bilateral, chronic, afebrile parotid tumours	122 „
Perlèche	168 „
Other conditions	13 „

Diffuse melanosis of the face was found in 5 of the patients with pellagra and the parotid tumours in 14. The authors do not consider that either of these conditions is related to pellagra as such, though the type of parotid tumours described is probably a manifestation of malnutrition.

Serum levels of nicotinic acid were variable and were not necessarily lower in patients with pellagra than in people without that disease. The authors do not therefore consider that such estimations are of diagnostic value.

The findings are tabulated. *H. J. O'D. Burke-Gaffney*

MIKES, A. Anemija kod pelagre. [**Anaemia due to Pellagra**] *Acta Med. Iugoslavica.* 1960, v. 14, No. 1, 1–19, 6 graphs. [20 refs.] English summary.

Between 1955 and 1958 the author, in Yugoslavia, made a haematological study of 52 cases of pellagra. The results are set out in tables and figures and full details of marrow biopsies are given for the 25 patients in whom these

were taken. Other studies included haemoglobin and blood cell estimations, blood picture, serum iron estimation, iron loading tests with and without the administration of nicotine acid or cortisone and Thorn's test.

In about two-thirds of the patients there was a mild to moderate anaemia; only 2 cases were severe, with haemoglobin (Sahli) below 40%. The anaemia was normochromic-normocytic in 80%, hypochromic-microcytic in 16% and hyperchromic-normocytic in 4%.

The marrow was usually hyperplastic, with preponderance of normoblasts. No case of megaloblastic marrow was found. Giant metamyelocytes were seen in 16 of the 25 patients examined and averaged 0·3–1·6%. Half of the patients had a moderate leucopenia and 80% a moderate thrombocytopenia: in 1 patient idiopathic thrombocytopenic purpura was also present.

In 36 patients serum iron was determined; it was below 100γ% in 62-65% of patients in the first few days of admission. 12 iron loading curves revealed good absorption and reduced iron stores; in 5 cases tested improvement in absorption was noticed after administration of nicotinic acid and cortisone, especially the latter.

The author stresses the multiplicity of deficiencies in erythropoietic factors in pellagra, *viz.* Fe, Cu, Co; various vitamins; proteins and amino acids, especially tryptophan. *H. J. O'D Burke-Gaffney*

SPRUE

Suarez, R. M. El pasado, el presente y el futuro del espru en Puerto Rico. **[Sprue in Puerto Rico in the Past, Present and Future]** *Bol. Asoc. Med. de Puerto Rico.* 1960, Jan., v. 52, No. 1, 1–22. [34 refs.]

A general review and discussion. [A Dr. Bailey K. Ashford Memorial Lecture.]

Sheehy, T. W., Rubini, M. E., Baco-Dapena, R. & Perez-Santiago, E. **Erythrokinetics in the Megaloblastic Anemia of Tropical Sprue.** *Blood.* 1960, May, v. 15, No. 5, 761–71, 4 figs. [28 refs.]

This is a study, by modern radioactive methods, of the function of the marrow in 10 untreated patients with tropical sprue in Puerto Rico. In brief, serum iron was normal, and the iron stores increased; total erythropoiesis was also increased, but this was not reflected in a reticulocytosis or in an increased utilization of iron. The rate of red cell destruction was increased in some patients, though not markedly, and was normal in 2, but owing to the reduced circulating red cell mass the total destruction per day was often less than normal—hence no bilirubinaemia.

The picture that emerges is of increased but ineffective marrow activity, with delivery of imperfect and therefore easily destructible cells to the peripheral circulation, the erythrocyte loss so caused setting up a vicious circle of increasing marrow embarrassment. This is reversed by folic acid. *Alan B. Raper*

HAEMATOLOGY

CARRINGTON, S. P. **The Plasma Fibrinogen Levels in Gambian Women and Young Children.** *West African Med. J.* 1960, June, v. 9, (n.s.) No. 3, 131–4, 1 fig. [14 refs.]

DEEGAN *et al.* [this *Bulletin*, 1957, v. 54, 602] in the Gambia showed that gamma globulin and fibrinogen levels of the plasma were increased in association with the relatively raised erythrocyte sedimentation level commonly encountered in Africans. The present author, in Fajara, Gambia, has studied plasma fibrinogen levels by means of a thrombin-nesslerization method in 55 Gambian women, 29 Gambian children under 2 years of age and 10 healthy Europeans. About one-third of the Gambians were exposed to malaria and the remainder were taking regular antimalarial drugs. Many of the subjects harboured parasitic worms, but they appeared to be in good health.

The mean plasma fibrinogen level in the Gambian was 342 mgm./100 ml. (range 160–530 mgm./100 ml.) and there was no important difference between women and children or between those exposed to malaria and those protected against it. The findings are shown in a figure. The Europeans had a mean level of 246 mgm./100 ml. (range 200–280 mgm./100 ml.). If normal values are taken to be 150–500 mgm./100 ml. it is evident that the levels in the Africans fell within the accepted range, but occupied a higher place in it, and were significantly higher than those of the Europeans.

The relationship of the fibrinogen level to the erythrocyte sedimentation rate is briefly discussed, with reference to the literature.

H. J. O'D Burke-Gaffney

CASLEY-SMITH, J. R. **The Haematology of the Central Australian Aborigine. IV. Haemoglobin, Erythrocyte Counts, Constants, Fragilities and Sedimentation Rates. Effects of Europeanization.** *Australian J. Exper. Biol. & Med. Sci.* 1960, Feb., v. 38, Pt. 1, 37–46. [36 refs.]

20 urbanized male Australian aborigines showed no difference from white people in haemoglobin and haematocrit percentages, red cell counts, and the derived indices. 30 nomadic male aborigines differed only in showing higher haemoglobin levels and haematocrits. But both the nomads and the urbanized aborigines showed higher sedimentation rates than Europeans.

[See also this *Bulletin*, 1958, v. 55, 1040.] *Alan B. Raper*

SMITH, D. A. & WEISS, C. Untersuchungen zur Pathogenese hypochrommegaloblastischer Anaemien im Sudan. [**Investigations on the Pathogenesis of Hypochromic and Megaloblastic Anaemias in the Sudan**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1960, v. 11, No. 1, 61–70, 4 figs. [20 refs.]

The haemoglobin concentration in the blood of a 100 allegedly healthy men aged 17–60 years in two different groups from small villages in the Sudan showed average levels of 9·5 (El Seraf) and 8·4 (El Rawashda) gm. per 100 ml. 103 male patients with hypochromic anaemia associated with intermediary

megaloblastosis in the bone marrow were treated with iron, folic acid and vitamin B12, or combinations of these. On re-examination after 10 days little response was noticed to treatment with folic acid and vitamin B12, though there was a better response to iron by itself, or to iron combined with either folic acid or vitamin B12.

The authors consider that the comparatively unsatisfactory response is due to the fact that in addition to specific deficiencies the anaemic men were suffering from a general protein deficiency. *H. Lehmann*

MacIver, J. E. & Back, E. H. **Megaloblastic Anaemia of Infancy in Jamaica.** *Arch. Dis. in Childhood.* 1960, Apr., v. 35, No. 180, 134–45, 9 figs. [51 refs.]

Megaloblastic anaemia is commoner in states of protein malnutrition in children than was previously thought. This is because the appearance of the peripheral blood is often normocytic, and it is only recently that bone marrow studies have been widely made. This is well illustrated by the present study. In Jamaica, 50 children with megaloblastic marrow changes were seen by the authors in 2½ years. Almost confined to the age period 9 to 18 months, with a sharp peak at 1 year, the anaemia corresponds in incidence with kwashiorkor, and is accompanied by signs of this syndrome.

Peripheral red blood cells were usually normocytic, occasionally hypochromic, rarely macrocytic. The marrow was either frankly megaloblastic or of "intermediate" type, though in a few children the abnormalities were very slight; however, giant metamyelocytes were always present. A feature peculiar to this anaemia (at any rate in Jamaican children) was the presence of erythropoietic activity in the liver—seen in 7 out of 12 biopsies, and 3 out of 6 autopsies. Response to folic acid (45 patients) was excellent, and to B12 (6 patients) wholly satisfactory, though sometimes an initial blood transfusion was needed, and infections often had to be treated.

The authors are not content to accept the success of specific therapy as proof of single deficiencies; and among other possible factors they pay special attention to lack of vitamin C. They note the virtual disappearance of reports of this anaemia from the United States after 1953, when ascorbic acid was introduced into most milk formulae, and they point to the importance of infections, especially intestinal, in precipitating anaemia, perhaps by increasing the need for and reducing the absorption of vitamin C. In their series there was one case of scurvy, which developed after a partial response to folic acid.

[The subject of megaloblastic anaemias of infancy is very fully dealt with in an excellent review by Zuelzer and Rutzky in *Advances in Pediatrics*, 1953, v. 6, 243.] *Alan B. Raper*

Tasker, P. W. G. **Treatment of Nutritional Megaloblastic Anaemia.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Mar., v. 54, No. 2, 171–7, 5 figs. [46 refs.]

48 Indian and Chinese patients in Kuala Lumpur, about two-thirds of them pregnant women, and all showing a megaloblastic marrow, were treated with

vitamin B12 and then folic acid, in doses sufficient to give a maximal response. The effect of the treatment was measured by the difference between the initial and the 15-day red cell count. With B12, half of the patients showed no response at all, and in the remainder the degree of response was unrelated to the initial red cell count. With folic acid, however, all patients responded, and the degree of response was related to the initial red cell count in the same manner as in the effective treatment of pernicious anaemia with B12. Moreover, previous treatment with B12 did not alter the subsequent response to folic acid, nor was combined treatment with the two drugs superior to the use of folic acid alone.

Alan B. Raper

SHAKIR, M. H. & SAIF, M. **Physiochemical Properties and Methods for the detection of Abnormal Haemoglobins.** *J. Ministry of Health.* Cairo. 1960, Apr.–May, v. 1, No. 4, 57–69. [40 refs.]

CIOCCA, F. La microcitemia ed il morbo di Cooley nei vari continenti e regioni della terra. [**Microcytaemia and Cooley's Anaemia in Different Continents and Regions**] *Igiene e San. Pubblica.* Rome. 1960, Jan.–Feb. & Mar.–Apr., v. 16, Nos. 1/2 & 3/4, 52–71; 216–41, 3 maps. [Numerous refs.] English summary.

An extensive review.

MODICA, R. & MACALUSO, Anna S. Inchiesta sulla presenza di emoglobine anormali in Tripolitania. [**Survey for Abnormal Haemoglobins in Tripolitania**] *Boll. Sanitario d. Tripolitania.* 1960, Jan.–Mar., 20–22, 2 figs.

The English summary appended to the paper is as follows:—

"Paper electrophoresis has been used to demonstrate the presence of abnormal haemoglobin in Tripolitania. Of 1,540 specimens tested 14 (0·9%) showed evidence of S haemoglobin (controlled by demonstration of sickling on slides). All the S trait carriers were negroes.

"No other abnormal haemoglobins were found."

VANDEPITTE, J. & DHERTE, P. Enquête sur les hémoglobines anormales à Stanleyville. [**A Study of Abnormal Haemoglobins at Stanleyville**] *Ann. Soc. Belge de Méd. Trop.* 1959, Oct. 31, v. 39, No. 5, 711–15. [12 refs.]

On examination of the haemoglobin of 1,000 African women at an antenatal clinic in Stanleyville, using paper electrophoresis, the authors found the following abnormal variants, all associated with Hb A:—Hb S, 278 cases; Hb D, 2 cases; Hb P, 1 case; Hb Stanleyville I, 1 case; Hb Stanleyville II, 1 case. It is notable that when other Belgian authors have encountered the D, P, and Stanleyville I and II variants, these have also been found in persons born in the Eastern Province. It is not surprising that Hb C was not found in the present survey since it has already been shown to be absent in parts of the territory nearer to the West African focus.

No case of sickle-cell anaemia was found among the 278 sicklers, and the authors remark that this confirms their previous opinion that only very rarely, under the conditions of life in the Congo, can a subject with sickle-cell anaemia attain the age of reproduction. *Alan B. Raper*

BECQUET, R., GASTEAU, Thérèse & HAPPI, C. La drépanocytose en Pays Bamiléké (Cameroun). Étude statistique. **[Sicklaemia in Bamiléké, West Cameroons]** *Bull. Soc. Path. Exot.* 1959, Nov.–Dec., v. 52, No. 6, 836–43.

The authors found a sickling rate of 8·3% in 543 members of the Bamiléké tribe in the West Cameroons, and compare it with the sickling rates found by others in the north (where it is lower) and in the east and south (where it is higher).

At the end of the paper a very remarkable finding is recorded; the sickling rate in 147 children under 12 was 17·68%, and in 396 adolescents and adults it was 4·79%. [This clearly has a significance that may, however, reflect technical, sampling, or genetic facts; the authors do not attempt to evaluate it.] *Alan B. Raper*

VELLA, F. & HART, P. L. de V. **Sickle-Cell Anaemia in an Indian Family in Malaya.** *Med. J. Malaya.* 1959, Dec., v. 14, No. 2, 144–50, 3 figs.

Sickle-cell anaemia, hitherto unknown in Malaya, is described in typical form in an Indian child of 11 years, whose grandparents had emigrated from Orissa. Sickling was present in the parents, and in 1 of the patient's 5 siblings, who also appeared to be a homozygote. *Alan B. Raper*

JONES, Barbara & KLINGBERG, W. G., with the technical assistance of Donna RENANDER. **A Study of Erythropoietin in Two Types of Hemolytic Anemia—Erythroblastosis Fetalis and Sickle Cell Anemia.** *J. Pediatrics.* St. Louis. 1960, June, v. 56, No. 6, 752–8. [29 refs.]

ERLANDSON, M. E., SCHULMAN, I. & SMITH, C. H. **Studies on Congenital Hemolytic Syndromes. III. Rates of Destruction and Production of Erythrocytes in Sickle Cell Anemia.** *Pediatrics.* Springfield, Ill. 1960, Apr., v. 25, No. 4, 629–44, 6 figs. [60 refs.]

Previous articles [this *Bulletin*, 1959, v. 56, 652; *Pediatrics*, 1959, v. 23, 462] analysed the state of balance between red cell production and destruction in thalassaemia and congenital spherocytosis. In the present work the same methods were used in the investigation of 8 children under 16 with sickle-cell anaemia, 2 with sickle-cell thalassaemia, and 2 with sickle-cell—haemoglobin-C disease. The experimental results require reading in full, but the following are salient points.

Patients with sickle-cell anaemia were found to have a markedly expanded plasma volume, in comparison with thalassaemia patients in whom the plasma

volume was but slightly expanded, and with congenital spherocytosis in which it was normal. Consequently the "peripheral" indices (such as Hb, packed cell volume) in the three diseases do not reflect the true relative degrees of anaemia. During crisis the plasma volume contracts, but it is not certain whether this causes the crisis (by concentrating erythrocytes in the small vessels), or is a result of, say, fever and the known inability of sicklers to secrete a concentrated urine; correspondingly, therapy by attempts at hydration have been disappointing, while the use of plasma expanders such as Dextran may be dangerous.

In contrast to previously held concepts which put the maximum possible haemopoietic response of the marrow at 6 to 8 times the normal, the authors find that effective erythropoiesis in sickle-cell anaemia may rise to 12·5 times the normal. Erythrocyte destruction could similarly rise to 20 times the normal, so that the "compensation index" (rate of production divided by rate of destruction) was in the region of 0·53 to 7·0.

The role of the spleen is discussed, and it is recalled that sickling erythrocytes survive better in a patient with an atrophic spleen than in a normal compatible recipient. 2 of the present sickle-cell anaemia patients had enlarged spleens, and in both cases sequestration of sickling red cells tagged with ^{51}Cr could be demonstrated in the spleen, whereas normal red cells were not so sequestrated. This agrees with the view that pathological atrophy of the spleen, or the removal of an enlarged spleen, is an advantage to anaemic sicklers, but the group was too small to make a definite statement possible.

In the two variants of sickle-cell disease studied, haemolytic effects were less severe than in the homozygous disease. *Alan B. Raper*

SULLIVAN, P. G. & BUTTERWORTH, C. E., Jr. **Sickle Cell Hemoglobin-C Disease treated by Splenectomy.** *Southern Med. J.* 1960, June, v. 53, No. 6, 792–5, 4 figs. [13 refs.]

The interest of this case report lies in the fact that an enlarged spleen was removed when the patient, a Negro boy, was 12 years old, and when the Hb C element in his illness had not been discovered. Very active erythrophagocytosis was noticed in splenic pulp smears. At age 19 the patient was symptomless and active, and was considered to have benefited from the splenectomy.

Alan B. Raper

MCCURDY, P. R., with the technical assistance of Mona M. GIESCHEN. **Clinical and Physiologic Studies in a Negro with Sickle-Cell Hemoglobin D Disease.** *New England J. of Med.* 1960, May 12, v. 262, No. 19, 961–4, 1 fig. [19 refs.]

AKSOY, M. **The Hemoglobin E Syndromes. I. Hemoglobin E in Eti-Turks.** *Blood.* 1960, May, v. 15, No. 5, 606–9. [18 refs.] **II. Sickle-Cell-Hemoglobin E Disease.** *Ibid.*, 610–13, 2 figs.

The first paper records that in a survey of 150 Eti-Turks (of whom 100 were from one village) Hb E was found in 3 subjects, once as a Hb S-E combination, and twice with Hb A. There were also 2 S-S and 41 A-S subjects.

The second paper describes briefly a family, the second to be recorded, which contained an individual with haemoglobin constitution S-E. This patient, with a moderate anaemia (Hb 8·4 gm./100 ml.) was more affected clinically than the 2 similar subjects described by the same author [this *Bulletin*, 1957, v. 54, 1232]. There is also a reference to the original family, bringing up to date the record of the offspring of an S-E male married to a normal woman; 5 of the children were A-E and 1 A-S. [Those who refer to the original description will find that when this family contained 5 children, 4 of them were recorded as A-S. This would appear to be a typographical error (for A-E); but the change makes no difference to the genetic conclusion, which is that whatever the indications, there is as yet no clear evidence in this family as to the allelism or otherwise of the genes for Hb E and Hb S.] *Alan B. Raper*

VENOMS AND ANTIVENENES

ONUAGULUCHI, G. O. **Clinical Observations on Snakebite in Wukari, Nigeria.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, May, v. 54, No. 3, 265–9, 1 fig.

Snake bite constitutes one of the main medical emergencies of Wukari, Nigeria. It is an area which lies between the rain forests of the south and the typical northern savannah. The commonest snakes in this area are the Viperidae.

20 victims of snake bite were admitted to the General Hospital between September 1956 and April 1957. There were 3 fatalities. Only one case was known to be due to cobra bite.

13 out of 18 subjects were bitten below the knee and 5 on the hand. 17 had swelling of the limb, and in all patients it appeared within 12 hours and was indurated, tender, non-pitting on pressure.

The importance of haemolytic anaemia in snake bite may have been exaggerated. In the present series there was no evidence of haemolysis. The importance of antivenene treatment is stressed. 5 case histories are given. The major problems of viperine bites were haematuria and circulatory collapse.

Philip Manson-Bahr

MAENO, H., MORIMURA, M., MITSUHASHI, S., SAWAI, Y. & OKONOGI. T. **Studies on *Habu* Snake Venom. 2b. Further Purification and Enzymic and Biological Activities of Hα-Proteinase.** *Japanese J. Microbiol.* 1959, July, v. 3, No. 3, 277–84, 5 figs. [16 refs.]

"1. Hα-proteinase was purified eight times from *Trimeresurus flavoviridis* venom using successive ammonium sulfate fractionation and calcium phosphate gel treatment. The preparation thus obtained was electrophoretically homogeneous.

"2. The purified Hα-proteinase was activated twofold by manganese chloride, although the crude venom was not affected, and inhibited by EDTA and cysteine.

"3. Hα-proteinase showed both lethal and necrotizing effects."

SHULOV, A. & AMITAI, P. Observations sur les scorpions: *Orthochirus innesi* E. Sim., 1910, ssp: *negebensis* nov. [**Observations on Scorpions: *Orthochirus innesi* Subspecies *negebensis***] *Arch. Inst. Pasteur d'Algérie*. 1960, Mar., v. 38, No. 1, 117–29, 3 figs. [11 refs.]

5 years' study in Israel, including laboratory observations, are reported for the scorpion *Orthochirus innesi* ssp. *negebensis* which is found under stones in desert regions, particularly in the south in the Jordan Valley and Dead Sea basin. Adults are 3 to 3·5 cm. long. A first sting suffices to kill a mouse, and subsequent stings are also lethal to them. [There is no report on effects on man.] There are detailed descriptions of the adults, the mating dance, and the birth of young. A female produces from 5 to 12 young at a time; the gestation period is about 6–15 weeks after mating, and parturition seems to take place in spring or autumn. The young once born (momentarily being an enveloped foetus) moult through 5 to 6 stages, being carried on the back of the parent female, sharing her prey and finally catching for themselves. Insects, adults and larval forms, are the usual diets. Completion of growth to adult takes [it seems] most of a year.

These scorpions coat, or varnish, themselves with secretions from their own gut and salivary glands, taking an hour to do so; they abstract the substance from their mouths with their pedipalps which, together also with the tail, smear the body. The scorpion finally holds its body clear of the ground, motionless, for 10 minutes after this toilet. The biological significance of all this is being studied. *D. S. Bertram*

BETTINI, S. Indagine sui casi di latrodectismo verificatisi negli anni dal 1938 al 1958 in alcune province d'Italia. Nota I. Provincia di Viterbo. [**A Survey of Latrodectismus Cases occurring during the Years from 1938 to 1958 in some Provinces of Italy. Note I. Province of Viterbo**] *Riv. di Parassit.* Rome. 1960, Mar., v. 21, No. 1, 21–38, 5 figs. [26 refs.] English summary.

The author has investigated the incidence of poisoning from the bite of the spider *Latrodectus tredecimguttatus* in the Province of Viterbo, Italy, during the years 1938–1958. He has studied the records of 15 local hospitals and other out-patient clinics and consulted local medical practitioners. He has found evidence of 394 patients having been treated for stings or bites by arthropods, and 51 persons having received treatment for snake bite during the same period. Some bites have been recorded as being from *Latrodectus*, no species being stated, and such cases are assumed to have been bites of *L. tredecimguttatus*; the same species of spider is believed to have been responsible where the record is of a bite by "tarantula", "arachnida" or a "doubtful" agent. These "highly probable" and "probable" histories add up to 234

presumed cases of latrodectism [but this total comes to 288 when the figures shown in Table 2 are added up].

The author discusses the geographical distribution of this spider in Viterbo province: cases of its bite showed an increased incidence during 1946–1948. The age-group of 15–30 years was most often involved and more men were bitten than women. The highest incidence was in June, July and August. The "victims" were usually bitten when working on the land and their treatment in hospital was of about 2 days, with recovery in every case. *J. Cauchi*

Li, J. R. **Methocarbamol in the Treatment of Black Widow Spider Poisoning. Report of a Case.** *J. Amer. Med. Ass.* 1960, June 11, v. 173, No. 6, 662.

"Methocarbamol (Robaxin) was used, in addition to treatment along previously accepted lines, in the treatment of a patient with black widow spider poisoning. Immediate relief was obtained. Further trials with this muscle relaxant should be made."

TOXOPLASMOSIS

Daoud, K. A. & Schwabe, C. W. **Sensitivity of Lebanese and Syrians to Toxoplasmin and to a Similar Antigen prepared from** *Leishmania tropica*. *Amer. J. Trop. Med. & Hyg.* 1960, Mar., v. 9, No. 2, 158–61. [13 refs.]

"1. Fifty-seven per cent of 129 Lebanese and Syrians tested with toxoplasmin gave positive reactions. Sixty-five per cent of the Syrians and 46 per cent of the Lebanese were positive. Seventy per cent of Moslems tested were toxoplasmin-positive as compared to 55 per cent of Christians.

"2. Of 51 individuals with leishmanial scars, 46 gave positive skin reactions to a toxoplasmin-like antigen prepared from *Leishmania tropica*. Nine individuals without leishmanial scars were also positive to the leishmanial antigen.

"3. There appeared to be no cross-sensitization to skin test antigens prepared from *Toxoplasma gondii* and *Leishmania tropica*.

"4. Presently available information concerning the epidemiology of toxoplasmosis and leishmaniases in Lebanon and Syria is briefly discussed with particular regard to recent observations."

Cook, I. **Toxoplasma in Queensland. IV. Serological Surveys of the Human Population.** *Australian J. Exper. Biol. & Med. Sci.* 1959, Dec., v. 37, Pt. 6, 581–92, 1 fig. [18 refs.]

Surveys of the incidence of human toxoplasmosis were conducted in Queensland [see also this *Bulletin*, 1960, v. 57, 636] and New Guinea, by means

of the examination of sera by the complement-fixation reaction and the dye test. The results are summarized in the table below.

These figures show clearly the increase in incidence during adolescence, but the author points out that the cytoplasm-modifying antibodies do not persist for as long as is usually thought; there is no steady rise in the infection rates in the later decades of life. Sera from aborigines showed two features of

Population	*Age-groups*	*Numbers effectively tested*		*Percentage Positive*	
		CF test	*Dye test*	*CF test*	*Dye test*
Normal white	Under 15	110	112	5	11
	15 and over	596	648	14	27
Suspected ocular toxoplasmosis	Under 15	36	39	31	38
	15 and over	79	94	27	39
Suspected glandular toxoplasmosis	Under 15	80	88	25	27
	15 and over	118	127	15	21
Aborigines, west coast northern	Under 15	—	72	—	21
	15 and over	—	23	—	22
central	Under 15	—	55	—	15
	15 and over	—	30	—	20
southern	Under 15	—	59	—	—
	15 and over	—	1	—	—
Aborigines, east coast	Under 15	—	19	—	42
	15 and over	—	30	—	37
Papuans	All ages	—	83	—	23

interest: the large number infected in childhood in the wet and tropical east coast district, and the entire absence of infection in childhood in the southern region where the rainfall is low.

Sera obtained from patients with chorioretinitis showed much higher rates in both tests than in the normal population; this was particularly evident in the youngest and oldest age-groups—the former no doubt because of congenital infections, the latter for an unknown reason. The figures for patients with suspected glandular toxoplasmosis were less striking than was expected and proved to be significantly higher only in the children.

P. C. C. Garnham

HAVLÍK, O. & HÜBNER, J. Výskyt toxoplasmózy v chovech králíků v ČSR. **[Occurrence of Toxoplasmosis in Rabbit Breeding Stocks in Czechoslovakia]** *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1960, v. 9, No. 1, 16–22. [39 refs.] English summary.

A serological investigation has been made of the incidence of toxoplasmosis among stocks of rabbits in Czechoslovakia bred for scientific purposes. Of 110 rabbits examined 104 (94·5%) gave a positive result in the dye test, in 2 instances in a titre of 1,048,576. Attempts to isolate the parasites from 8 rabbits by the inoculation of mice were successful in 2 instances. The strains isolated were not highly virulent for mice, and required several passages for complete adaptation. The authors draw attention to the possibility of domestic rabbits acting as a reservoir of infection, particularly of laboratory workers and pregnant women.

D. J. Bauer

BENIRSCHKE, K. & RICHART, R. **Spontaneous Acute Toxoplasmosis in a Marmoset Monkey.** *Amer. J. Trop. Med. & Hyg.* 1960, May, v. 9, No. 3, 269–73, 6 figs.

CHAPARAS, S. D. & SCHLESINGER, R. W. **Plaque Assay of *Toxoplasma* on Monolayers of Chick Embryo Fibroblasts.** *Proc. Soc. Exper. Biol. & Med.* 1959, Nov., v. 102, No. 2, 431–7, 7 figs. [11 refs.]

The authors have adapted the plaque method for the quantitative assay of toxoplasms. For this purpose chick embryo fibroblast monolayers were grown on Petri dishes in Hanks solution containing 20% horse serum and 5% chick embryo extract. After 15–24 hours the growth medium was removed and the monolayers were inoculated with 0·5 ml. of *Toxoplasma* suspension from the peritoneal exudate of infected mice. When the organisms were adsorbed (at 37°C.) the monolayers were covered with nutrient agar. By the 4th day, the toxoplasms produced on the monolayer necrotic plaques, and it was shown that there was a correlation between the number of organisms plated and the number of plaques, each of which is produced by a single parasite. While the plaques contained numerous toxoplasms, which were infective to mice and could be passaged to new monolayers, no organisms were present in areas free of plaques.

It was found that Hanks balanced salt solution containing chick embryo extract (5–50% concentration) preserves 80–100% plaque forming activity of the organisms for 3–4 hours, and 50–60% for 6 hours.

The advantage of this method—in comparison with mouse infection—is that (a) it represents a direct cell count; (b) plaques can be detected in 4–5 days, and (c) abundant growth of toxoplasms can be produced at will.

C. A. Hoare

BEVERLEY, J. K. A. **Ocular Toxoplasmosis.** Reprinted from *Human Toxoplasmosis.* 1960. Copenhagen: Munksgaard. 159–65, 6 figs. on 2 pls. & 3 graphs. [10 refs.]

"The clinical types of ocular toxoplasmosis are outlined. Attention is drawn to the occurrence of pathological lesions before birth in some cases and after birth in others. A mechanism is suggested which may account for these two kinds of reaction. The significance of laboratory findings is discussed and their greater diagnostic value in younger patients is emphasised. The possibility of in utero neutralisation of toxoplasms by passively acquired antibodies is mentioned and a case passing through a negative phase is presented. Experimental work suggesting that passively acquired antibody can neutralise toxoplasms is described. Remote complications and their relation with stress are noted. Treatment of humans and experimental animals is discussed and the synergic effect of chemotherapy [4,4' diaminodiphenylsulphone (DDS)] and cortisone is shown."

DERMATOLOGY AND FUNGUS DISEASES

COHEN, L. B. **Idiopathic Lymphoedema of Ethiopia and Kenya.** *East African Med. J.* 1960, Feb., v. 37, No. 2, 53–74, 15 figs. [20 refs.]

In this paper the author sets out to prove that the common conditions of lymphatic oedema below the knees and lymphostatic verrucosis ("mossy" foot) seen in Ethiopia and Kenya [this *Bulletin*, 1935, v. 32, 182; 1949, v. 46, 283] result from long-standing lymphatic obstruction due to hypoplasia of the lymphatic vessels in the leg below the knee.

He bases his thesis on the study of 32 patients, 19 from Ethiopia and 13 from Kenya. In some, both the oedema and "mossy" foot were present, in others, only the oedema. It was more frequent in males (23 in this series). There was no evidence that it is hereditary, contagious or confined to certain tribes. It tended to appear initially in the second decade of life.

The usual mode of onset is with swelling on the dorsum of the foot; this gradually extends up to the knee. Later, the "moss" or verrucosis may appear on the foot but this never involves the sole. There is a tendency for it to become bilateral but it rarely starts in both legs together, and does not become so gross as to warrant the term elephantiasis. At first pitting on pressure, the skin later thickens to such an extent that no impression can be made on it. Folds of skin appear at the ankles and these usually become infected. The condition is painless, and there is no fever if the condition is uncomplicated, nor is there true anaesthesia in the affected area. All attempts to find any form of infective agent, bacterial, fungal or metazoan failed.

At operation it is found that the skin may be 1 inch in thickness and is firmly attached to the white subcutaneous tissue, which is moist with lymph when first exposed. The superficial fascia is firmly attached to the deep fascia, but this is not adherent to the underlying muscles which are normal. Apart from occasional eosinophilia, the blood count is normal. The Kahn test was not done but urine examination and plasma protein estimations showed no changes from normal.

Having concluded that the condition was not infective, the author set out to demonstrate the state of the lymph channels in the affected legs. The methods

of visual lymphangiography, serial injection and retrograde dissection, microscopy of lymph vessels and X-ray lymphangiography were employed in a few selected patients and results all showed very little spread of dye through superficial lymph plexuses, poor passage of lymph in the smaller lymph vessels and absence or marked hypoplasia of the main lymph channels below the knee. Control examination of normal limbs showed the usual arrangement of lymphatics and veins.

Treatment in the early and mild form may consist of bandaging or this combined with scraping of the mossy area. For the established disease, however, excision of the affected tissues is the method of choice. All the thickened tissue is removed and the muscles are laid bare. Split skin grafts are applied about 2 weeks later, the grafts coming from the normal skin of the thighs. It was found that the affected skin could not be successfully used for the grafting. In the 22 patients coming to operation there were no deaths, and 9 were assessed as having a good result, 4 as fair and the remaining 9 as being improved. Follow-up was not possible since patients would not return unless they wished for more treatment.

The author suggests that lymphostatic verrucosis always follows a period of oedema in legs in which the lymphatic vessels are hypoplastic, and that repeated traumata and mild infections consequent upon wearing no covering on the feet lead to a relative inadequacy of the lymph drainage first appearing in the second decade of life. He thinks that the wearing of boots may lessen the disease and that this, together with prolonged use of antibiotics in the early stages may prevent progress of the condition. *J. R. Rose*

CAMPINS, H. **Epidemiological Aspects of Deep Mycoses in Venezuela.** *Mycopathologia.* The Hague. 1960, June 30, v. 13, No. 1, 25–32, 1 map. [24 refs.]

TROPICAL OPHTHALMOLOGY

EISELEN, H. H. & GEAR, J. **The Occurrence of Trachoma in the Eastern Caprivi Strip of South West Africa.** *South African Med. J.* 1960, May 28, v. 34, No. 22, 456–8.

"The Caprivi Strip is a tongue of land about 250 miles long joining the territory of South West Africa to the territories of Northern and Southern Rhodesia, the junction occurring on the Zambesi River west of the Victoria Falls. . . .

"Clinical examination of a representative sample of the population of the Eastern Caprivi Strip showed that 64% had evidence of eye infections resembling trachoma. The highest incidence was in infants up to 2 years old; the 2–14 year age group had an incidence of 69%, the females of the age group 15–60 years an incidence of 63%, and the male group of 15–60 years an

incidence of 53%. Few cases showing entropion cicatrization or other late sequelae were found.

"Microscopic examination of 60 conjunctival smears taken from the inhabitants of one area showed the presence of typical inclusion bodies in 3 cases, and of particles resembling the elementary bodies of trachoma in another 3, giving an incidence of 10% of active infections. The true incidence of the disease is therefore considerably greater. Of interest also was the relatively small proportion which showed bacteria resembling Koch Weeks bacilli. The low incidence of pathogenic bacterial infections may account to some extent for the small number of cases showing entropion cicatrization, and other late sequelae of trachoma.

"This study has confirmed that trachoma occurs and is prevalent in the population of the Eastern Caprivi Strip."

WHITNEY, Elinor & GEAR, J. **Laboratory Studies of Eye Infections in South Africa with special reference to the Virus of Trachoma.** *South African Med. J.* 1960, May 28, v. 34, No. 22, 451–3.

The methods used in the investigation of suspected cases of trachoma in South Africa are described. *S. P. Bedson*

CUTHBERTSON, E., SMITH, D. M. & GEAR, J. **Laboratory Studies of Eye Infections in South Africa. The Properties of the Virus of Trachoma.** *South African Med. J.* 1960, May 28, v. 34, No. 22, 453–6.

By using their northern Transvaal strain of virus the authors attempted to infect the conjunctiva of guineapigs, rabbits, calf, ram and vervet and rhesus monkeys, with negative results. They also failed to infect week-old white mice by the cerebral and peritoneal routes [unlike HURST and REEVE; see *Bull. Hyg.*, 1960, v. 35, 818]. Attempts to cultivate this strain of trachoma virus in the cells derived from a variety of human (amnion, conjunctiva, eye, HeLa and KB) and animal (kidney, bone marrow, testis and lymphoid tissue of vervet monkey, lung of mouse, kidney of dog and *Mystromys*, heart of guineapig and chick embryo) tissues, were abortive except for cultures made with the testes of vervet monkeys which showed some multiplication of the virus.

S. P. Bedson

SCOTT, J. G., GEAR, J., CUTHBERTSON, E. & SMITH, D. M. **Trachoma Studies: Transmission of Jane Furse Virus to a Human Volunteer.** *South African Med. J.* 1960, May 28, v. 34, No. 22, 450–51.

The authors report having reproduced trachoma in a volunteer with a strain of virus isolated from an African girl in the north-eastern Transvaal. The virus was re-isolated and clinical cure was obtained by the local application of erythromycin. 6 months after recovery the volunteer's eye was successfully re-infected. *S. P. Bedson*

HANNA, L., JAWETZ, E., THYGESON, P. & DAWSON, C. **Trachoma Viruses isolated in United States. 1. Growth in Embryonated Eggs.** *Proc. Soc. Exper. Biol. & Med.* 1960, May, v. 104, No. 1, 142–5.

The report of the isolation of a virus, with the appearance of those of the psittacosis-lymphogranuloma group, from patients with trachoma in the United States, confirms what has been achieved in other parts of the world [this *Bulletin*, 1959, v. 56, 95]. Yolk sac inoculation of the embryonated egg was the method employed. 6 strains were isolated. They produced a follicular conjunctivitis in *Macaca cynomolgus* and with one trachoma was reproduced in a human volunteer. The susceptibility of the eggs—obtained commercially—to trachoma virus varied unaccountably and dramatically; this did not appear to be due to antibiotics in the feed of the egg-producing birds.

S. P. Bedson

CHANG, Hsiao-Lou, CHIN, Hsiu-Ying & WANG, K'o-Ch'ien. **Experimental Trachoma in Human Volunteers produced by Cultured Virus.** *Chinese Med. J.* Peking. 1960, Mar., v. 80, No. 3, 214–21, 8 figs. on 2 pls.

The authors report the production of experimental trachoma in 2 volunteers by means of 2 of the 14 strains of virus which they isolated from human trachoma by egg inoculation. One of these strains had been passed 9 times in eggs and had been 10 weeks away from man, the other had been isolated 18 months previously and been through 19 egg passages. Both strains were recovered by egg inoculation. The experimental disease was readily controlled by local Aureomycin. The volunteers were 2 of the authors, but the names are not given.

S. P. Bedson

ADELSTEIN, A. M. **Measurements in a Field Survey of Trachoma before and after Treatment.** *South African Med. J.* 1960, May 28, v. 34, No. 22, 446–9.

"The results of a field survey by two ophthalmic surgeons of trachoma at 4 schools are analysed according to (1) prevalence; (2) the variation in diagnosis of one individual surgeon at different times and the variation between different surgeons; and (3) the effect of treatment with 3 certain antibiotics.

"The mean prevalence of trachoma as indicated by the two surgeons' diagnoses before treatment was 25% up to age 10 years, 13% at age 11–14 years, and 11% at age 15–18 years.

"After the surgeons had consulted on a standard, the disagreement was nevertheless substantial, being 13% of all the children examined. The difference in prevalence found by the surgeons was 2·6% at the first examination. In a series of 134 cases examined twice in the same afternoon by both surgeons, there was close agreement both within and between surgeons. Six months later and without another consultation about standards, the difference in prevalence diagnosed by them was 8·7% and was highly significant.

"Three of the schools had received antibiotic treatment and the 4th a placebo treatment. One surgeon found significant reductions at all the schools, including

the control school, presumably because he had changed his approach on account of a subjective expectation of an effect of treatment. He found more highly significant changes at the treated schools than at the control school. The other surgeon found no significant change at the control school, a highly significant decrease at one treated school and decreases at the other treated schools which were not significant. A combined measurement of agreed cases is in favour of the effectiveness of the treatment, particularly at one of the schools.

"There is evidence that, in the absence of treatment, trachoma is a chronic disease and that there is a minimum of re-infection at school ages, during which the prevalence gradually diminishes as the children get older."

See also p. 1038, WEISS & DRESSLER, **Centrifugation of Rickettsiae and Viruses onto Cells and its Effect on Infection.**

See also p. 1110, BEVERLEY, **Ocular Toxoplasmosis.**

D'HAUSSY, R. & UEMURA, K. A propos de l'origine génétique des lésions choriorétiniennes observées chez les onchocerquiens. [**Concerning the Genetic Origin of Chorioretinal Lesions in Patients with Onchocerciasis**] *Maroc Méd.* 1960, Apr., v. 39, No. 419, 460–65. [16 refs.]

The authors consider it logical that the ophthalmoscopic appearances of the choroidoretinal lesions observed in patients with onchocercal infection have given rise to the hypothesis that they could have a genetic origin. It is probable that all ophthalmologists have wondered about their origin when they saw them for the first time. They claim that greater experience of these lesions shows that:

(1) they are met with in co-existence with onchocerciasis in Africa and in America;
(2) they have clinical characteristics which allow them to be distinguished from the tapeto-retinal heredo-degenerations described by SORSBY;
(3) in an endemic milieu they have a frequency which increases with the degree of infection and are, for all practical purposes, not encountered among African hospital patients other than in persons with onchocerciasis.

The authors have produced some epidemiological evidence concerning infected African patients in support of their views.

It seems not impossible to the authors that these tapeto-retinal degenerations can be observed in other affections, especially in other filarial affections. Their paper appears to suggest that Sorsby has not fully explored the possibility that the tapeto-retinal degenerations which he considers to be of genetic origin are due to some systemic condition acting upon the choroid and retina from an exogenous source.

[However, the reviewer is unable to accept the statement that these tapeto-retinal degenerations which have been observed in onchocercal patients could be readily distinguished from similar conditions described by Sorsby and thought by him to be of genetic origin. So far as the reviewer is concerned

they are, ophthalmologically speaking, one and the same condition. He is also satisfied that Sorsby's explanation of their origin, *i.e.* that they are of genetic origin, is the correct one.

It seems to the reviewer that this controversy has not been brought any nearer solution by the paper under review which should, however, be brought to the notice of all workers in this field.] *D. P. Choyce*

MISCELLANEOUS DISEASES

Fox, H. C. & Miller, D. S. **Ackee Toxin: a Riboflavin Antimetabolite?** [Correspondence.] *Nature*. 1960, May 14, v. 186, 561–2, 1 fig. [10 refs.]

Rats fed on a Jamaican diet containing a large amount of ackee fruit failed to grow and lost weight, although the diet was rich in protein and adequate in vitamins and minerals, and this was probably due to an ackee toxin. When riboflavin was added to the diet, the growth rate was improved, although the diet contained amounts of riboflavin known to be sufficient for rats. This suggests the presence of an antimetabolite of riboflavin.

A substance, hypoglycin A, has been extracted from ackees and is toxic when given subcutaneously, but the toxic effects may be alleviated by injection of riboflavin.

It is pointed out that severe signs of riboflavin deficiency were noted in most cases of illness in which ackee was implicated [this *Bulletin*, 1953, v. 50, 562] and that the incidence of the condition has fallen in recent years during which consumption of wheat flour has risen. *R. Passmore*

Walker, A. R. P. & Grusin, H. **Coronary Heart Disease and Cerebral Vascular Disease in the South African Bantu. Examination and Discussion of Crude and Age-Specific Death Rates.** *Amer. J. Clin. Nutrition*. 1959, May–June, v. 7, No. 3, 264–70. [33 refs.]

These authors discuss critically the supposed dearth of coronary heart disease among the South African Bantu. They present data from the Department of the Census of the Johannesburg Public Health Department showing that the average age of these people is much younger than that of some western countries. Only 2% of the population are over 65 and only 12% over 45. Corresponding figures for comparison among white South Africans are 7% and 24%, while those for the U.S.A., England and Wales and France are still higher. Although the crude death rate from coronary disease among the urban Bantu is one-twentieth of that of the local white population, the specific rate at ages 45–64 is only one-seventh, and is nearly the same as the death rate at these ages in France, Italy and Japan. Death certificates for Bantu are legally required only in large centres of population, and even here it is doubtful if more than 90% of deaths are reported. The reliability of Bantu mortality rates is further affected by the migrant nature of the population and the

frequent uncertainty as to their age. There is a need to ascertain to what extent the diet and way of life of the Bantu who die of coronary heart disease had been westernized.

The certified death rate for cerebral vascular disease at ages 45–64 among the Johannesburg Bantu is of the same order as that among the local white population.

[This paper is of value in pointing out the difficulties of assessing the real risk of ischaemic heart disease among the Bantu. It is not clear, however, what inferences can be drawn from some of the figures quoted by the authors. No analysis is made of either deaths or populations for men or women separately, yet the sex-ratio of the immigrant urban Bantu must be at least as important as their age-distribution in determining the incidence of the disease.]

[See also this *Bulletin*, 1959, v. 56, 1279.] *A. S. Fairbairn*

WEBB, J. K. G. **Aetiology of Tropical Eosinophilia.** *Indian J. Child Health.* 1960, May, v. 9, No. 5, 227–30.

The primary objective of this investigation was to demonstrate organisms in tissue obtained from patients with tropical eosinophilia. With few exceptions all patients had absolute eosinophil counts above 4,000 per cmm., gave a positive filarial complement-fixation test (FCFT) and showed a therapeutic response to diethylcarbamazine and the blood was consistently negative for microfilariae. Lung, liver and lymph nodes were obtained from different cases for biopsy. No less than 5,000 serial sections from lung tissue of 4 patients were searched in detail under the high power lens. Scattered irregularly throughout were nodules involving 20–30 alveoli which showed consolidation and were distended with eosinophils enmeshed in fibrin. Some of them showed a central eosinophil "abscess", in which portions of microfilariae were found; others showed peripheral fibrosis and central giant-cell granuloma. Others, again, contained deeply eosinophil-staining hyaline material surrounding fragments of degenerating larvae, resembling the bodies described by MEYERS and KOUWENAAR as MK bodies [this *Bulletin*, 1939, v. 36, 838]. In all the lung material 5 almost complete microfilariae were found, and in 17 nodules there were recognizable fragments of microfilariae.

As a number of workers have reported significant hepatomegaly in tropical pulmonary eosinophilia [see *ibid.*, 1951, v. 48, 583; 1957, v. 54, 1471; 1959, v. 56, 1282], open liver biopsy was performed in 5 children with hepatomegaly and tropical lung infiltration. Open biopsy was also performed in 2 children without pulmonary infiltration, one with an isolated hepatosplenomegaly and one with hepatomegaly and lymphadenopathy. In all these 7 children the liver was found to be slightly enlarged, and scattered over the surface were whitish dots, 2–5 mm. in diameter and varying in number from 4 or 5 up to hundreds. On microscopic examination the structure of these nodules was essentially similar to those seen in the lungs. In some 3,000 serial sections one almost complete microfilaria was found in the centre of an aggregate of eosinophils.

Lymph-node biopsy was performed on 14 children. In 3 of these lymphadenopathy was the presenting symptom. The nodes measured up to 3 cm. in diameter. In 2 of the children there was no evidence of any pulmonary

involvement. In 7 cases, 2 without and 5 with, lung involvement, the nodes contained eosinophil aggregates and granulomata. On the cut surface, grey or brownish nodules, about 1 mm. in diameter, were apparent. The histology of these nodules was essentially similar to those seen in lung and liver, and in all of them portions of microfilariae were found in some eosinophil aggregates.

Saline preparations were allowed to stand at room temperature. They were then centrifuged, and wet drop preparations and stained smears made from the deposits. Microfilariae were found in 6, and in 5 of them live parasites were seen in wet drops. These were all of the *Wuchereria bancrofti* type.

These findings strongly suggest that all these lesions of tropical eosinophilia represent a direct reaction to an invading parasite. With all the features described in common, the fact that the tissues involved varied between lung, liver and lymph nodes, either alone or in combination, suggests that the term tropical eosinophilia be reserved for those eosinophilias where filarial infection is proved or assured. At present it has not been possible to determine the species of filaria responsible for tropical eosinophilia.

Philip Manson-Bahr

FESTENSTEIN, H. **Adenocarcinoma of the Breast in a South African Bantu Boy aged Fourteen.** *South African Med. J.* 1960, June 18, v. 34, No. 25, 517–18, 4 figs. [22 refs.]

MCKENNA, C. M., Jr. & HERMANN, R. E. **Ainhum—Occurrence of a Case in Northern Ohio.** *J. Amer. Med. Ass.* 1960, July 2, v. 173, No. 9, 1015–17, 4 figs.

"A case of ainhum was reported from Northern Ohio, an area in which the condition is rare. The patient, a Negro man, had spent three months on the island of Tinian in the South Pacific during World War II. Amputation of the affected toe resulted in prompt healing. A review of the various measures advocated for treatment of this condition leads us to recommend amputation as the most effective form of therapy at present."

EMMONS, Patricia & MCLENNAN, H. **Some Observations on Tick Paralysis in Marmots.** *J. Exper. Biol.* 1960, June, v. 37, No. 2, 355–62, 3 figs. [10 refs.]

"1. Observations have been made on marmots paralysed by the attachment of the ixodid tick *Dermacentor andersoni* Stiles.

"2. Acetylcholine synthesis by excised tissues from paralysed animals is unaffected.

"3. Conduction in both motor and sensory nerve fibres is markedly reduced. It is likely also that the excitability of neurones of the spinal cord is diminished.

"4. There are changes in the electrocardiogram suggestive of a slowed rate of auricular and ventricular depolarization and repolarization."

PARASITOLOGY: GENERAL

BIAGI F., F. **Parasitosis en pediatria.** [Parasitic Diseases in Paediatrics]

This book was reviewed on p. 866.

RUBIN, E. & ZAK, F. G. *Pneumocystis carinii* **Pneumonia in the Adult.** *New England J. of Med.* 1960, June 30, v. 262, No. 26, 1315–17, 3 figs. [26 refs.]

A case in New York.

VAN DEN AKKER, S. & GOEDBLOED, Else. **Pneumonia caused by** *Pneumocystis carinii* **in a Dog.** *Trop. & Geograph. Med.* Amsterdam. 1960, Mar., v. 12, No. 1, 54–8, 9 figs. [19 refs.]

"Large numbers of *Pneumocystis carinii*, DELANOË 1912, were found in the lungs of a one-year-old dog that died from interstitial pneumonia. The various stages of development of the parasite are described. It was the first time a spontaneous pneumocystis-pneumonia was observed in an animal."

ENTOMOLOGY AND INSECTICIDES: GENERAL ZOOLOGY

[Papers on the toxic effects of insecticides in man are abstracted in the *Bulletin of Hygiene* under the general heading of Occupational Hygiene and Toxicology.]

WIGGLESWORTH, V. B. [M.D., F.R.S.] **The Control of Growth and Form: a Study of the Epidermal Cell in an Insect.** pp. vi + 140, 47 figs. & 8 pls. 1960. Ithaca: Cornell University Press, New York. London: Oxford University Press, Amen House, Warwick Square, E.C.4. [21s.]

DOBY, J. M., RAULT, B. & DAVID, F. *Theobaldia* (*Culicella*) *litorea* (Shute 1928) et *Anopheles* (*Anopheles*) *algeriensis* Théobald 1903, dans l'ouest de la France. Contribution à l'étude écologique de ces deux espèces. [**The Ecology of** *Theobaldia litorea* **and** *Anopheles algeriensis* **in Western France**] *Ann. Parasit. Humaine et Comparée.* 1960, v. 35, Nos. 1/2, 174–87, 6 figs. [28 refs.]

On their evidence of numerous breeding places on the Atlantic seaboard of southern France, the authors consider *Theobaldia litorea* as a species of

western temperate regions in Europe rather than centred on the Mediterranean. It has one generation a year, and breeds often in fairly brackish, reedy water along the coast. Three breeding places of *Anopheles algeriensis* and one biting adult were also found on this western seaboard, confirming previous records for the region. Much reedy vegetation and brackish water characterized the breeding places. This species occurred with *Th. litorea.*

There are several photographs of breeding places and a table of physico-chemical and vegetational features of waters in which these two, and other species of mosquito, were taken. *D. S. Bertram*

GOMA, L. K. H. **The Swamp-Breeding Mosquitos of Uganda: Records of Larvae and their Habitats.** *Bull. Entom. Res.* 1960, Apr., v. 51, Pt. 1, 77–94. [25 refs.]

Permanent swampland occupies some 2,500 square miles of Uganda and, during the rains, seasonal swamps of about the same area are also found. In this paper records are given of 92 species of mosquito found breeding in the swamps, 37·4% of the total number of species and varieties of mosquito known from Uganda. Only 26 species, however, have been found to be restricted to the swamps for breeding. Neither *Anopheles gambiae* nor *A. funestus* breed extensively in these swamps but the opening up of this type of country by cultivation may produce an increased incidence of malaria.

[See also this *Bulletin*, 1959, v. 56, 241.] *B. R. Laurence*

SUZUKI, Y., YONEKAWA, S., OKADA, I. & ONISHI, A. **[Observation of Mosquitoes on Aoshima, Ehime Prefecture]** *Shikoku Acta Med.* 1960, Feb., v. 16, No. 1, 140–42, 1 map. [13 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"The authors collected and observed, during one year from May in 1955, mosquito larvae which bred on Aoshima, an island, 4 km in circumference. This island in the Inland Sea is located 14 km off Nagahama-cho, Ehime Prefecture. Collected mosquitoes belong to 7 species (4 Genera). Those of the species Aedes albopictus were the most numerous, those of Culex pipiens, Aedes togoi, Culex vorax and Armig. subalbatus come next in number, while those of Culex pallidothorax and Anoph. hyrcanus were the least. Contrary to our expectations we found many mosquitoes of the species Culex vorax. This fact is remarkable.

"In the life history of the Culex vorax, the animals from which this mosquito sucks blood are yet uncertain. Its ecology is also obscure. Because of its rather big form and inactive nature, and because its activities are almost limited to night, it can be assumed that it sucks blood from animals of dull movement during night. From investigations of animals on this island it is known that, in contrast to a large number of birds (including domestic fowls, sparrows, crows, etc.) any other mammals than 2 dogs, 30 cats, 30 pigs and rats do not live on this island. Because suction of blood from animals which can move quickly even at night is difficult for mosquitoes, it may be concluded that mosquitoes perhaps suck blood from birds at night."

BOWMAN, M. C., ACREE, F., Jr., SCHMIDT, C. H. & BEROZA, M. **Fate of DDT in Larvicide Suspensions.** *J. Econom. Entom.* 1959, Dec., v. 52, No. 6, 1038–42, 1 fig. [10 refs.]

The authors have investigated some of the factors which determine the availability of DDT (in aqueous suspensions) to mosquito larvae. The behaviour of the insecticide under different conditions was studied mainly by means of radiometric techniques.

The results revealed, in the first instance, that DDT does settle from suspensions at a concentration of 1 p.p.m. but not at 0·01 p.p.m. At both concentrations, however, DDT was rapidly dispersed so that two minutes after preparation of the suspensions 39% to 56% of the insecticide was recovered from the walls of the containers. This phenomenon was explained in terms of the hydrophobic properties of DDT.

At 0·01 p.p.m. more than 50% of the DDT originally present in the suspension was lost after 24 hours. Evidence is provided for considering this loss to be due to codistillation—that is, the DDT was volatalized together with the water.

[See also SCHMIDT and WEIDHAAS, this *Bulletin*, 1960, v. 57, 854.]

B. C. Fine

FAIRCHILD, G. B. & HERTIG, M. **Geographic Distribution of the *Phlebotomus* Sandflies of Central America (Diptera: Psychodidae).** Reprinted from *Ann. Entom. Soc. of America.* 1959, Mar., v. 52, No. 2, 121–4. [18 refs.]

SUKHOVA, M. N., SHNAIDER, Y. V., YEROFEYEVA, T. V., ZLATKOVSKAIA, Y. V. & KUKLINA, N. P. **Comparative Assessment of DDT, BHC and Chlorophos in Combating Synanthropic Flies inhabiting Decaying Organic Matter and the Prospects for their Destruction.** *J. Microbiol., Epidemiol. & Immunobiol.* 1959, v. 30, No. 6, 76–84, 3 figs.

BOJANOWSKA, Anna & WÓJCIAK, Zofia. Stan oporności na DDT much (*Musca domestica* L.) w Polsce w latach 1953–1958. **[Resistance to DDT of Flies (*Musca domestica* L.) in Poland in 1953–1958]** *Przegląd Epidemiol.* Warsaw. 1960, v. 14, No. 1, 67–81, 3 figs. [32 refs.] English summary.

Resistance to DDT among house-flies (*Musca domestica*) was first observed in Poland in 1952, and between 1953 and 1958 the authors carried out trials in the Warsaw area and other parts of Poland in order to determine the degree of resistance of flies captured in the field. Filter paper was soaked in 4% DDT emulsion in the proportion of 1 cc. of emulsion per 100 sq. cm., corresponding to a deposit of 4 gm. of DDT per square metre. Batches of 30 flies were exposed for 1 hour on the dried paper in Petri dishes; they were then removed and examined over a period of 24 hours. The proportion of flies surviving after this time was taken as the resistance index. During the period of the observations 406 tests were carried out on a total of 13,589 flies. The mean resistance index ranged from 0·08 to 0·77 and the maximum value from

0·19 to 1. The highest values were found in 1955; a fall was then observed which was attributed to the increasing use of Gammexane [gamma-benzene hexachloride]. The use of the resistance index in planning fly control measures is discussed. DDT could still be used with values below 0·25, but when the index exceeds 0·5 it should be replaced by other insecticides. *D. J. Bauer*

REIFF, M. & BEYE, F. Stoffwechselvorgänge bei sensiblen und resistenten Fliegen unter Einfluss der DDT-Substanz. [**Metabolism of Susceptible and Resistant Flies subjected to Treatment by DDT**] *Acta Tropica*. Basle. 1960, v. 17, No. 1, 1–47, 7 figs. [99 refs.]

The authors work in the group led by Dr. R. WIESMANN at the Geigy Laboratories in Basle. This rather long paper (which is offered as a tribute on Dr. Wiesmann's 60th birthday) expounds the outlook of this team on DDT resistance. After the remarkable discovery and isolation of DDT-dehydrochlorinase in Professor Kearns's laboratory, most American workers have seemed to consider this a practically complete explanation of DDT resistance in house-flies. The Swiss workers, however, have been compiling evidence to suggest that numerous factors contribute to the immunity of resistant flies.

The present paper describes a large number of simple biochemical tests conducted on flies from 2 resistant (R) and 3 susceptible (S) strains. These include tests for DDT-dehydrochlorinase, measurement of proteins, amino acids and of lipoids, also of respiration of flies. The tests were made on untreated and on treated flies; also estimations were made from various parts of the flies (tarsi, haemolymph, nerve ganglia) as well as whole flies.

The enzyme which degrades DDT was found in all strains, though more abundantly in the R strains. After exposure to DDT the tarsi of S flies seemed to have increased facility to degrade DDT.

In most of the other investigations there were few differences of significance between untreated resistant and normal fly strains (proteins and amino acids, carbohydrates, respiration rates, catalase, esterase). In regard to lipoids there were apparently significant differences in amount (more in R strains) and quality. A considerable number of differences between S- and R-strain flies were found after treatment with DDT. However, these were not easy to interpret. Thus, proteins in S tarsi increased and in R tarsi decreased after treatment; but the reverse was true of the haemolymph. Increased respiration in S flies (but not in R flies) was found after treatment, in agreement with other workers. [But the obvious explanation—increased activity due to the nerve stimulation of DDT—does not seem to be mentioned.]

In a long and rather complex discussion, the authors ascribe resistance to: (i) a series of barriers in R flies, such as reduced penetration, lipoid storage reservoirs in the tarsal cuticle and elsewhere, DDT-destroying enzyme and possibly membranes; (ii) the fact that R flies have a stable metabolic system which compensates for any disturbance due to a toxicant and restores the normal equilibrium of various enzyme-substrate systems. In contrast, S flies have their whole metabolic balance disturbed by DDT, one system involving another. Thus, it is suggested that with the greatly increased respiration the normal lipoid metabolism in S flies may be insufficient and other substrates are involved, thus tending to depletion of vital reserves. *J. R. Busvine*

BAUMHOVER, A. H., HUSMAN, C. N., SKIPPER, C. C. & NEW, W. D. **Field Observations on the Effects of releasing Sterile Screw-Worms in Florida.** *J. Econom. Entom.* 1959, Dec., v. 52, No. 6, 1202–6, 1 fig.

In 1954 the screw-worm, *Callitroga hominivorax*, was successfully eradicated from the island of Curaçao, off the coast of Venezuela, by releasing males rendered sterile by irradiation [this *Bulletin*, 1956, v. 53, 1395]. As an intermediate step between this operation and a projected eradication programme in a much larger area in the south-eastern United States, an experiment was conducted over a 2,000 square mile area in Florida. The activity of wild and released screw-worm populations was evaluated by exposing goats wounded in the shoulder, for egg mass collections. Fertile egg masses were recognized by the presence of empty shells and newly-hatched larvae the following day, while sterile egg masses retained their original appearance.

The insects were irradiated as $5\frac{1}{2}$- to $6\frac{1}{2}$-day-old pupae with 6,200 to 8,300 r gamma rays of cobalt-60. The emerging adults were fed on honey and released within 24 hours of complete emergence. The cartons containing the adults (500 per carton) were opened and dropped from a low-flying aeroplane. Over the major part of the test period, the weekly release rate averaged 548 males per square mile. Egg mass collections dropped from 41 per goat pen in the release area during the first two months of the experiment to as low as 8 in the 12th week and the sterility increased steadily until it approached 70%.

The 100% sterility observed in Curaçao was never obtained in the Florida experiment, probably owing to the considerable fly movement into the test area from outside the release area. However, surveys following the releases indicated a marked decline in screw-worm incidence in the treated area and demonstrated the effectiveness of the experiment. *M. G. R. Varma*

MACKERRAS, I. M. **The Tabanidae (Diptera) of Australia. III. Subfamily Pangoniinae, Tribe Scionini and Supplement to Pangoniini.** *Australian J. Zool.* 1960, Apr., v. 8, No. 1, 1–152, 40 figs. on 4 pls. & 185 text figs. [42 refs.]

ARTHUR, D. R. **Ticks. A Monograph of the Ixodoidea. Part V. On the Genera *Dermacentor*, *Anocentor*, *Cosmiomma*, *Boophilus* and *Margaropus*.**

This book was reviewed on p. 866.

See also p. 1032, HARINGTON, **A Simple Apparatus for the Artificial Feeding of *Rhodnius prolixus* (Hemiptera, Reduviidae).**

See also p. 1032, HARINGTON, **Studies on *Rhodnius prolixus*: Growth and Development of Normal and Sterile Bugs, and the Symbiotic Relationship.**

SETZER, H. W. **The Spiny Mice (*Acomys*) of Egypt.** *J. Egyptian Pub. Health Ass.* 1959, v. 34, No. 3, 93–101.

MISCELLANEOUS PAPERS

GELFAND, M. **Proud Record. An Account of the Health Services Provided for Africans in the Federation of Rhodesia and Nyasaland.** 67 pp., illustrated. 1960. Salisbury: Govt. Printer, for the Federal Information Dept.

In his preface the author remarks that "I have spent what might be considered the best part of my medical career with the indigenous people . . ." It is this fact and the sympathy and understanding with which he has approached the people that makes Gelfand's work so compelling. He has often written about the beliefs and customs of the Africans which relate to health and disease, and in the first chapter of the present work he recapitulates the outlines of their interpretation of illness as a result of influences from the spirit world, commonly summoned by witches.

In succeeding chapters he traces the history of the introduction of European medicine into Central Africa, and its development from the time of Livingstone onwards, and discusses the administrative health services, training of African auxiliaries, preventive services, research, statistical research, housing, and the progress made in 5 years of federation.

It is unnecessary to say that great changes have been made during this century; vast numbers of dispensaries and clinics have been established throughout the 3 countries of the federation, and many large and well equipped hospitals now exist which are beyond the scale of anything conceived 50 years ago. Many men were associated with these advances, among whom Dr. A. P. Martin and Dr. Richard Morris are singled out; the reviewer takes particular pleasure in the credit given to Dr. J. F. C. Haslam who for a time was Assistant Director of the Bureau of Hygiene and Tropical Diseases, and to Dr. H. S. Stannus who for many years acted as Sectional Editor for the *Tropical Diseases Bulletin*.

It is not possible to abstract this monograph briefly. It is an account of medical services—largely curative but increasingly preventive—initiated by official bodies, missions, and private practitioners, and the author is aware of the enormous problems still to be encountered. In the early days malaria and other fevers were too often the fatal occupational diseases of doctors, and later practitioners working in comparative safety may pay a tribute to those pioneers who took their lives in their hands. But they and their successors worked well; it is to their credit that the Africans come very freely indeed, and with confidence, to accept treatment based on a culture not their own.

Gelfand gives a mass of detailed information on all these subjects, and his account should be read in full. *Charles Wilcocks*

SLOME, C., GAMPEL, B., ABRAMSON, J. H. & SCOTCH, N. **Weight, Height and Skinfold Thickness of Zulu Adults in Durban.** *South African Med J.* 1960, June 11, v. 34, No. 24, 505–9, 1 fig. [19 refs.]

REPORTS AND SURVEYS

EAST AFRICAN MED. J. 1960, Mar., v. 37, No. 3, 131–70, 1 fig. [Numerous refs.] **The Third Conference of East African Branch of the Society of Medical Officers of Health. July 2, 1959.**

The presidential address, entitled *The Way Ahead*, was given by N. R. E. FENDALL (pp. 131–139). He sketched the history of public health from 1830 until the present when the main interest is in the concepts of health and epidemiology. He urged the study in East Africa of ill-health in the place where it develops and should be combated, namely the home. Curative medicine is popular and on it social medicine must be built by the team-work of all public health personnel. To this end vital statistics are essential and success will depend on health education.

Peri-Natal Mortality, by G. J. GOOSEN (pp. 140–145), was defined as the ratio per 1,000 births of foetal and neonatal deaths, including stillbirths, from the 28th week to 7 days after birth. In the African Maternity Hospital, Nairobi, this rate over the last 12 years was 117 per 1,000. The main causes were prematurity (35%), anoxia (17·3%) and birth injuries (10·2%). Threatened premature labour could be halted in 70% by mapanesin and the pregnancy would go to term. Premature babies treated with norethandrolone gained weight twice as fast as controls and their mortality declined.

Nutrition and Farm Planning in Kenya was discussed by O. H. KILLEN (pp. 146–157). The diet, particularly in the Highlands, is unbalanced, bulky, deficient in protein and animal fat, and poor in minerals. Suggested remedies have considered national rather than personal and family needs. Farm planning should be concerned with the maintenance and income of the individual and his dependants. A farm of 6 acres could provide a balanced diet for a family. The problems of land tenure, soil exhaustion and erosion require solution, and education will be needed to popularize newly introduced foods.

J. de M. VINK gave an address on *A Health Service for the Plantation Industry* (pp. 158–161). Kenya's economy depends on farms and plantations, with a hired labour force, on which health standards could be raised. Labour should be stabilized and not casual. Medical examination should consist of urine and stool examination and miniature chest X-ray examination of workers and families. Prophylactic vaccines should be given at the required intervals for continued protection. Refuse disposal, adequate housing and a daily meal for the family, first aid and ambulance facilities should be provided.

Dental Health in Kenya was discussed by M. M. WILLIAMSON (pp. 162–166). His address was a plea for establishing preventive measures before curative dentistry became overwhelmed. In developing areas dental health deteriorated in ratio to the closeness of relationship with immigrant peoples and their diet. A school service, largely staffed by dental hygienists, is needed for the dental education of children. The best results of such a service would be obtained from work among the indigenous people before their dental condition deterioriated.

W. OUKO'S title was *Discussions on Approaches to the African Mind in Effecting Health Education and Hygiene Matters* (pp. 167–170). Here an African explains how health education can be made effective in a primitive African environment. It must be related to African culture, and it could be

disseminated by political leaders and the village administration. Preventive measures are long-term and must be introduced through curative medicine which has the confidence of the people. Interesting examples are given of the way in which new ideas could be popularized by accepting and adapting traditional attitudes and behaviour. *T. H. Davey*

EAST AFRICAN MED. J. 1960, Mar., v. 37, No. 3, 171–237, 1 fig. [20 refs.]

The Fourth Conference of the East African Branch of the Medical Officers of Health. January 29, 1960.

A very informative address on *Health Centres in Kenya*, given by N. R. E. FENDALL (pp. 171–185) opened the symposium which was intended to give a picture of the organization, development and functioning of Kenya's health centres. The concept of the health centre, designed for English conditions, has been modified and adapted to the physical, social and economic environment in Kenya. Its function is to take curative, preventive and promotive services into the home where health education is most effective.

Rural Health Centre Projects in North Nyanza are described by J. M. D. ROBERTS (pp. 186–203). Dispensaries near health centres have been closed and are used for visiting clinics, while remote areas are served by mobile units. Details of capital and recurrent costs of health centres are given and it is emphasized that they reduce expenditure by diverting patients from hospitals. A complete service can be given only for a distance of 5 miles around the centre or to a population of 20,000; greater coverage reduced efficiency. Training health centres in rural areas are now needed to improve practical and domiciliary experience.

O. H. KILLEN described *Rural Health Centres in Kiambu* (pp. 204–216). Though there are only 4 health centres for a population of 350,000 in an area of 420 square miles, a basic structure has been laid down by associating welfare and other health workers with all development activities, especially women's clubs. There is a weekly clinic at the centre and on the other 4 days the health team has a mobile programme. Children's crêches are organized and domiciliary midwifery is practised. Tuberculosis is a serious problem, with an incidence of positive sputum in the Kiambu population of 4·2 per 1000 [wrongly shown as 4·2% by Killen. The figure 4·2 per 1000 for positive sputum is reported on p. 36 of the WHO/UNICEF Tuberculosis Survey of Nairobi, reviewed in *Bull. Hyg.*, 1960, v. 35, 558]. This is being combated by early domiciliary treatment.

D. R. HAUPT gave an address on *Urban Health Centres in Kenya* (pp. 217–223). Health centres, which have been exclusively rural so far, should be established in the towns before the curative services are overwhelmed. They should provide curative, preventive and promotive services under one roof, and their most important work should be done by the health visitors. Domiciliary midwifery should be developed. An urban health centre would require capital expenditure of £5,200, recurrent expenditure of £3,129 and revenue might amount to £1,360.

The work of *A Mobile Health Unit Amongst the Masai* was described by C. CACHIA (pp. 224–231). These people are pastoral and nomadic or semi-nomadic and they still retain their traditional ideas and mode of life. The

static curative units in existence were inadequate and preventive medicine did not function except during epidemics. Special problems in the area were high infant mortality, venereal disease and anthrax incidence (though anthrax mortality was only about 3%). The organization of a mobile unit is described. Curative medicine has had good results but preventive services are lagging, though tuberculosis and trachoma control are making progress.

G. WOLFENDEN gave an address on *Mobile Health Units in West Suk* (pp. 232–236). 3 mobile units provide the main medical and health services for this pastoral and nomadic tribe. Certain centres are visited regularly every 2 or 4 weeks. The main emphasis is still on treatment but its growing popularity is making other advances possible. Health education is carried on by talks to the audience of onlookers.

This series of papers will prove invaluable to those concerned with the establishment or development of health centres. It describes all aspects of their organization and work. *T. H. Davey*

SPITZ, A. J. W. **Health and Morbidity Survey, Seychelles, 1956–57.** *Bull. World Health Organization*. Geneva. 1960, v. 22, No. 5, 439–67, 8 figs.

The objects of this survey were to obtain basic information on general morbidity including dental and nutritional status, incidence of intestinal and other easily diagnosable diseases, and growth curves of children. The findings were to be correlated together and with social and environmental conditions.

Only about 40 of the 92 islands of the Seychelles are inhabited. The population is derived from the original French settlers, the African slaves they imported, and Indian and Chinese merchants. Intermarriage has rendered racial differentiation difficult. The main tropical scourges are absent, mostly for lack of their vectors. The common epidemic respiratory infections are found, but the main problems are the intestinal diseases, particularly helminthiasis and protozoal infections.

The field work was carried out largely by 2 people only, a doctor and a laboratory technician. Local sanitary inspectors and public health nurses were used as auxiliary workers, preparing lists, interpreting and smoothing public relations. Thus at any moment the team consisted of 4 people. Public cooperation was won by a propaganda campaign, by ensuring that no wages were lost by attendance, and by offering free treatment for infectious diseases.

It was necessary to take a sample of the population. The unit of sampling was the house; every seventh house throughout the islands was selected, giving a total of 5,766 inhabitants. A sanitary inspector was sent out a week ahead to inform and list the prospective subjects, at the same time giving them a paper cup for a stool specimen to be collected on the examination day. Out of 5,589 subjects, in only 2 cases were stools missed. All findings were transferred to individual punch cards for sorting.

Results of the survey are given in great detail. Age distribution shows the preponderance of young persons typical of high birth and child death rates. Infant mortality rates, tabulated from "before 1900", show a drop from 200 to 90. Further tables give fertility rates and information about stillbirths and miscarriages. Growth curves are much the same as those for U.S.A. children until weaning, but afterwards both weights and heights are lower than those

of American children. Nutrition tables and graphs indicate that roughly half of the population are thin or emaciated, and analyse the percentages by age and sex. Haemoglobins and erythrocyte sedimentation rates are also analysed. 82·9% of the population have over 80% haemoglobin. 26·5% have perfect teeth and 35·8% have 6 or more carious teeth. Environmental sanitation and social status are analysed according to overcrowding, condition of housing and quality of latrines. Analysis of intestinal parasitism indicates that the hook-worm and amoebic infection rates increase gradually with age, while that of *Ascaris* sinks after a peak in the 5 years age-group. Soil pollution was investigated, and found to be correlated with the nocturnal use of chamber pots. Mycotic infections, hernias, eye diseases, syphilis and the sickle-cell trait (1·5% of the total population) were also investigated.

[A great deal of information on a variety of subjects is set out in this paper. Perhaps the most valuable aspect is its detailed description of how such a small team accomplished so much: the methods could serve as a pattern for similar surveys.] *B. B. Waddy*

BOOK REVIEW

GOODWIN, Leonard [M.B., B.S., B. Pharm., B.Sc.] & DUGGAN, Anthony J. [M.D., D.T.M. & H.] **A New Tropical Hygiene.** 148 pp., 57 figs. 1960. London: George Allen & Unwin Ltd., Ruskin House, Museum Street, W.C.1. [5s. 6d.]

This little book is intended for teenage schoolchildren and elementary teacher training institutions. In the simplest and clearest language it gives an account of the nature of living things, human anatomy and physiology, and then of the processes of disease and of individual tropical diseases, their nature, transmission and prevention. The diagrams, specially those illustrating the transmission of individual diseases, are clear and pass on the intended message. Altogether the book fulfils its intentions admirably at a very low price, and can be recommended for use in schools anywhere in under-developed countries.

It is a reviewer's duty to compare such a book with any predecessor, and TAYLOR'S *A Textbook of Hygiene for Teachers in Africa* [this *Bulletin*, 1957. v. 54, 900] should be mentioned. This also was well written and gave a clear and comprehensive account, at not quite such a modest price. For schoolchildren the book under review is recommended. A teacher whose knowledge is derived solely from it may be caught out by supplementary questions from the brighter members of the class, and will be wise to arm himself doubly against this contingency by possessing both these useful little manuals. *B. B. Waddy*

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